

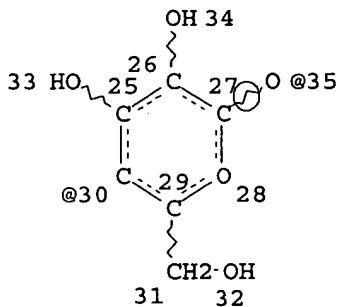
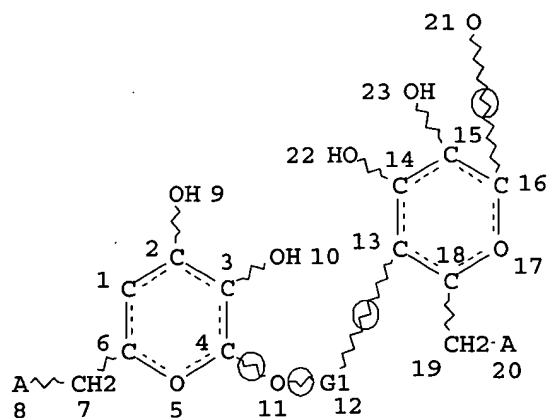
cyclode: rxnsites + text

Crane 09/339,818

June 23, 2004

=> d que
L4

STR



REP G1=(0-3) 30-11 35-13

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

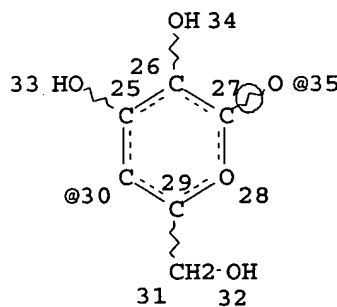
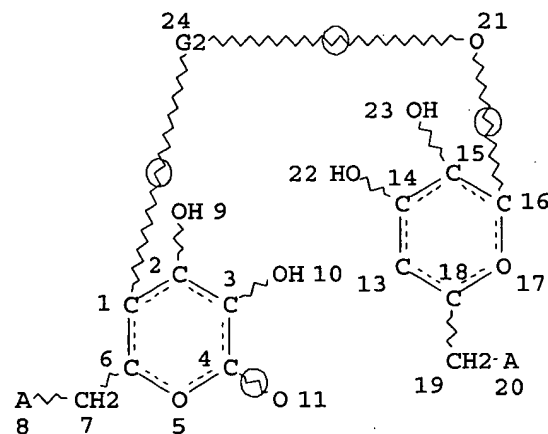
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE

L6 21339 SEA FILE=REGISTRY SSS FUL L4

L7 STR



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NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

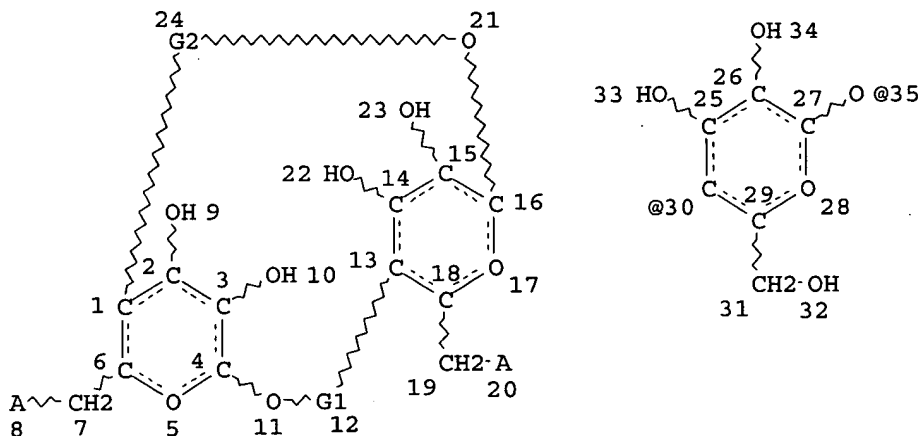
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NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE

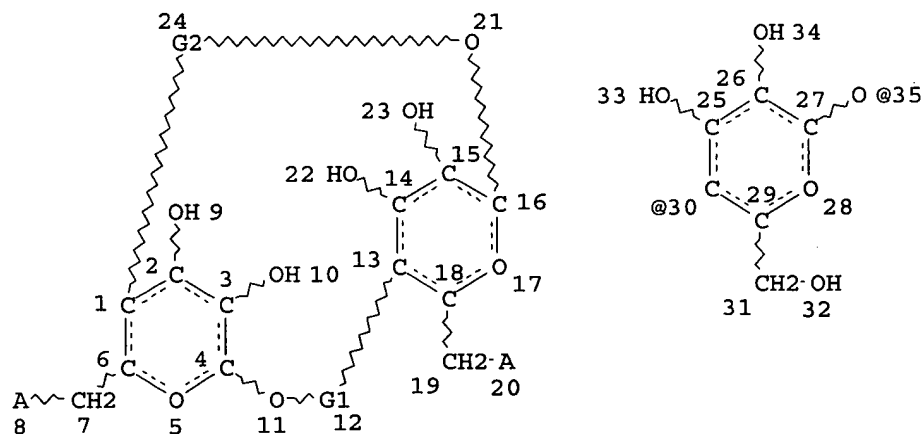
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L11 STR



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REP G2=(2-4) 30-21 35-1
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE
L13 17536 SEA FILE=REGISTRY SUB=L9 SSS FUL L11
L14 STR



REP G1=(0-3) 30-11 35-13
REP G2=(5-6) 30-21 35-1
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

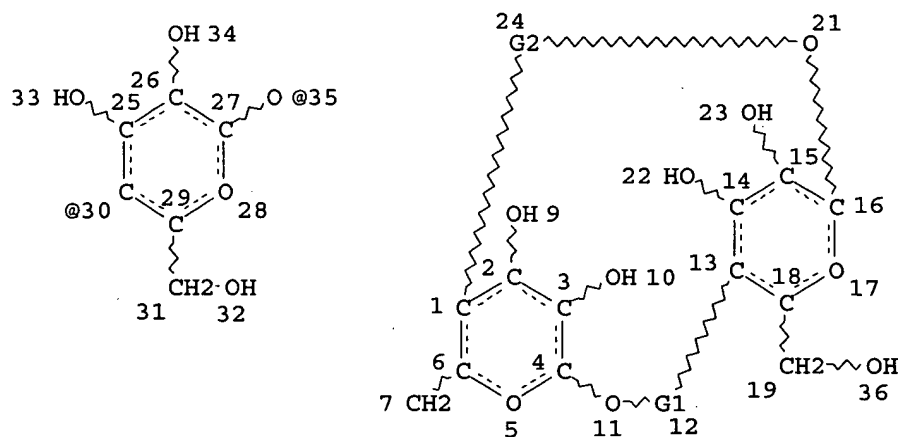
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE

L15 13536 SEA FILE=REGISTRY SUB=L9 SSS FUL L14

L16 17980 SEA FILE=REGISTRY ABB=ON PLU=ON L13 OR L15

L43 STR



REP G1=(0-3) 30-11 35-13

REP G2=(2-4) 30-21 35-1

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

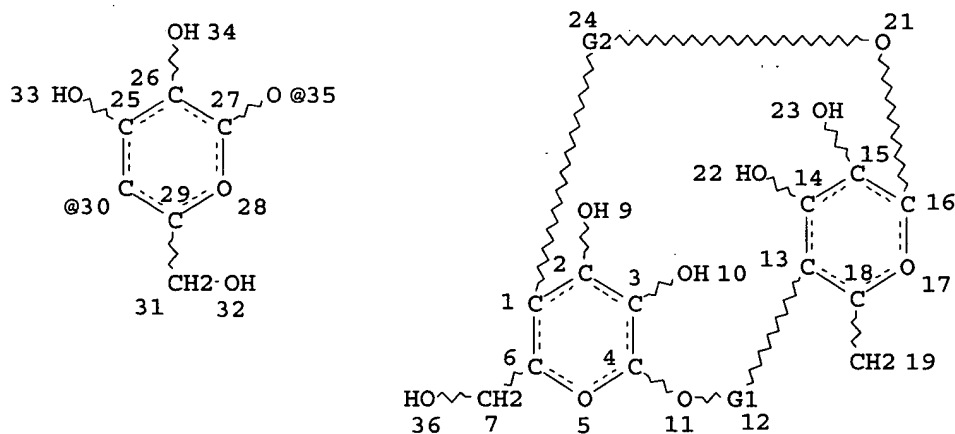
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RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE

L44 STR



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REP G2=(2-4) 30-21 35-1

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

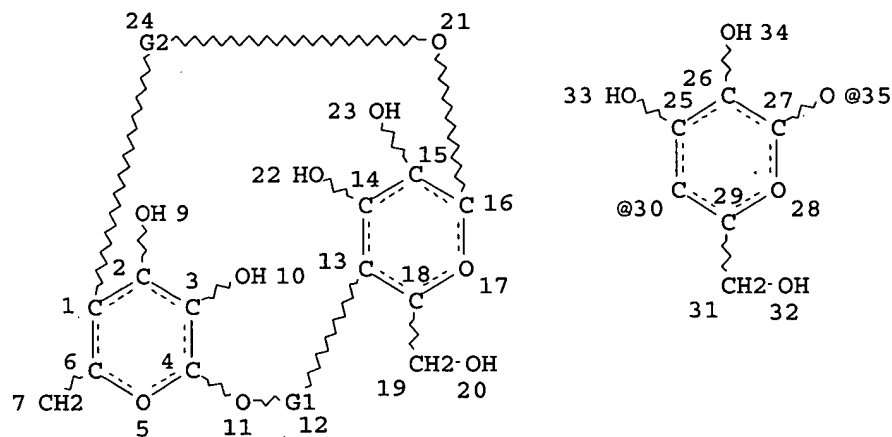
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 34

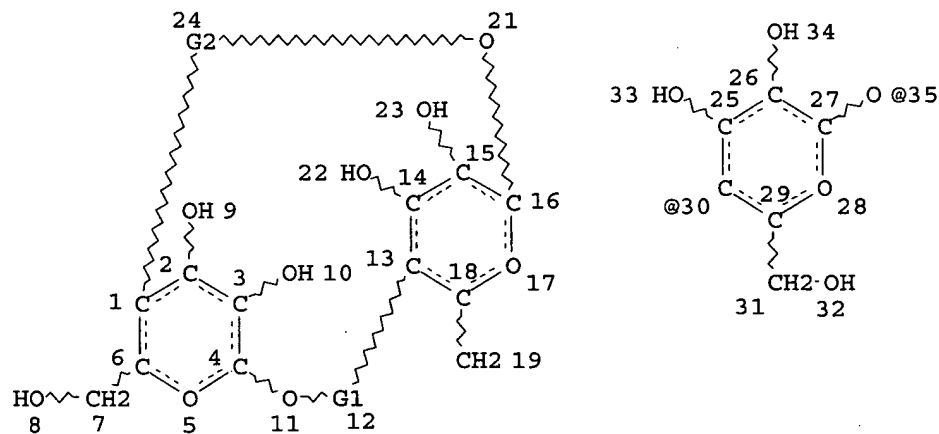
STEREO ATTRIBUTES: NONE
L45 STR



REP G1=(0-3) 30-11 35-13
REP G2=(5-6) 30-21 35-1
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE
L46 STR



REP G1=(0-3) 30-11 35-13
REP G2=(5-6) 30-21 35-1
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE

L47 17075 SEA FILE=REGISTRY SUB=L9 SSS FUL L43
L48 17075 SEA FILE=REGISTRY SUB=L9 SSS FUL L44
L49 13423 SEA FILE=REGISTRY SUB=L9 SSS FUL L45
L50 13423 SEA FILE=REGISTRY SUB=L9 SSS FUL L46
L51 17105 SEA FILE=REGISTRY ABB=ON PLU=ON (L47 OR L48 OR L49 OR L50)
L52 1212 SEA FILE=REGISTRY ABB=ON PLU=ON L16 NOT L51
L54 126 SEA FILE=HCAPLUS ABB=ON PLU=ON L52 (L) (RACT OR RCT OR RGT)/RL

L55 ~~14~~ SEA FILE=HCAPLUS ABB=ON PLU=ON L54 AND ?POLYMER?

=> d l55 ibib abs hitind hitstr 1-14 :

L55 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:331929 HCAPLUS

DOCUMENT NUMBER: 140:363027

TITLE: Cyclodextrin-modified **polymer** carriers
coupled to biorecognition molecules for drug delivery

INVENTOR(S): Bellocq, Nathalie C.; Davis, Mark E.; Pun, Suzie Hwang

PATENT ASSIGNEE(S): Insert Therapeutics, Inc., USA

SOURCE: PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004032862	A2	20040422	WO 2003-US31991	20031008
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

US 2004109888 A1 20040610 US 2003-681745 20031008

PRIORITY APPLN. INFO.: US 2002-417373P P 20021009

AB The application discloses cyclodextrin-modified materials for carrying drugs and other active agents, such as nucleic acids. Compns. are also disclosed of cyclodextrin-modified materials that release such active agents under controlled conditions. The invention also discloses compns. of cyclodextrin-modified **polymer** carriers that are coupled to biorecognition mols. for assisting the delivery of drugs to their site of action. A number of examples are given for preparation of cyclodextrin-PEG derivative

conjugates.

IC ICM A61K

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 33, 35

IT Polyoxyalkylenes, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(carboxylated, reaction products with cyclodextrins;

Amel's over link

- cyclodextrin-modified **polymer** carriers coupled to biorecognition mols. for drug delivery)
- IT Drug delivery systems
(carriers; cyclodextrin-modified **polymer** carriers coupled to biorecognition mols. for drug delivery)
- IT Inclusion compounds
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclodextrin-modified **polymer** carriers coupled to biorecognition mols. for drug delivery)
- IT Nucleic acids
Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclodextrin-modified **polymer** carriers coupled to biorecognition mols. for drug delivery)
- IT Drug delivery systems
(prodrugs; cyclodextrin-modified **polymer** carriers coupled to biorecognition mols. for drug delivery)
- IT Platelet-derived growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β , nucleic acid encoding; cyclodextrin-modified **polymer** carriers coupled to biorecognition mols. for drug delivery)
- IT 52-90-4, L-Cysteine, reactions 677-24-7, Methyl dichlorophosphate 2094-72-6, 1-Adamantanecarbonyl chloride 4411-25-0, 1-Adamantyl isocyanate 4942-47-6, 1-Adamantaneacetic acid 6240-11-5, 1-Adamantaneethanol 9002-98-6, Polyethylenimine 9057-02-7, Pullulan 17768-41-1, Tricyclo[3.3.1.1^{3,7}]decane-1-methanamine 25322-68-3D, carboxylated, reaction products with cyclodextrins 42503-45-7, Pentaerythritol ethoxylate 64913-54-8 **76700-72-6** 98443-27-7 129434-27-1 393781-65-2 401514-72-5 438490-98-3 681286-95-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclodextrin-modified **polymer** carriers coupled to biorecognition mols. for drug delivery)
- IT 768-94-5DP, Tricyclo[3.3.1.1^{3,7}]decane-1-amine, reaction products with carboxylated polyethylene glycol 70539-42-3P 85419-94-9P 152310-58-2P 214042-86-1P 438490-97-2P **614744-04-6P** 672333-69-6P **681286-88-4P** 681286-92-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cyclodextrin-modified **polymer** carriers coupled to biorecognition mols. for drug delivery)
- IT 2094-72-6DP, reaction products with pullulan 4411-25-0DP, reaction products with branched polyethylene glycol/pullulan 4942-47-6DP, Tricyclo[3.3.1.1^{3,7}]decane-1-acetic acid, reaction products with branched polyethylene glycol/polyethylenimine 9002-98-6DP, Polyethylenimine, reaction products with cyclodextrin derivs. 9002-98-6DP, reaction products with cyclodextrin tosylate 9057-02-7DP, Pullulan, reaction products with adamantyl isocyanate 98443-27-7DP, reaction products with PEI 101652-40-8DP, reaction products with carboxylated polyethylene glycol 438490-98-3DP, reaction products with RGD peptide 614744-05-7DP, reaction products with adamantylmethanamine 614744-05-7P 681286-87-3P 681286-89-5P 681286-90-8P 681286-91-9P 681286-93-1P 681286-94-2P 681286-96-4P 681286-97-5P 681286-98-6P 681286-99-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclodextrin-modified **polymer** carriers coupled to biorecognition mols. for drug delivery)
- IT **76700-72-6**
RL: RCT (Reactant); RACT (Reactant or reagent)

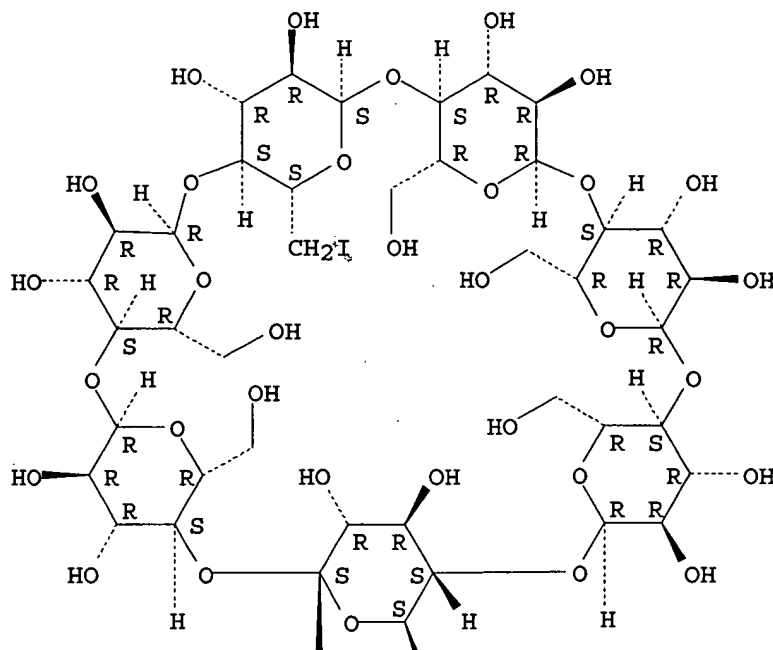
(cyclodextrin-modified **polymer** carriers coupled to
biorecognition mols. for drug delivery)

RN 76700-72-6 HCAPLUS

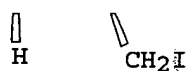
CN β -Cyclodextrin, 6A,6D-dideoxy-6A,6D-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT 614744-04-6P 681286-88-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

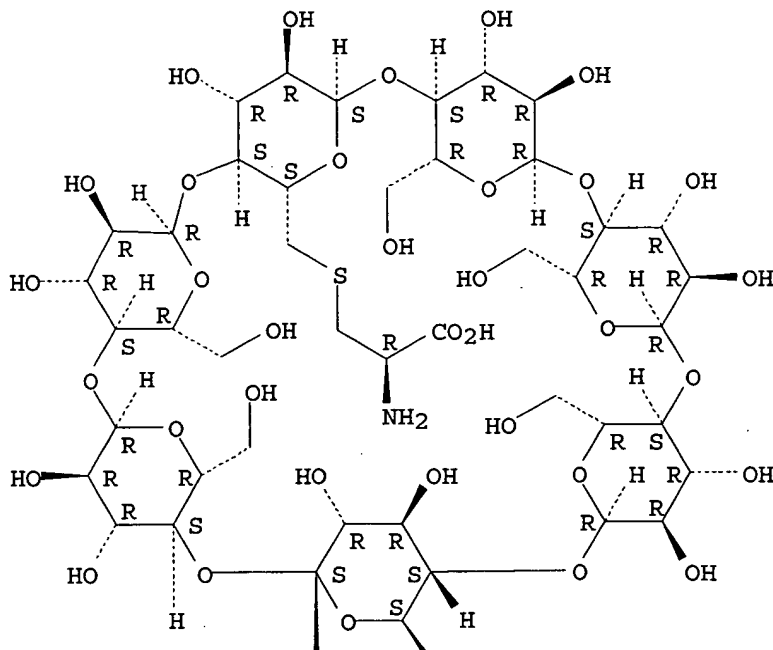
(cyclodextrin-modified **polymer** carriers coupled to
biorecognition mols. for drug delivery)

RN 614744-04-6 HCAPLUS

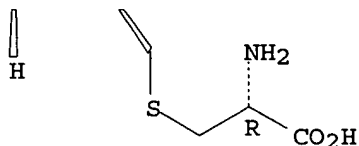
CN L-Cysteine, S,S'-(6A,6D-dideoxy- β -cyclodextrin-6A,6D-diyl)bis- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



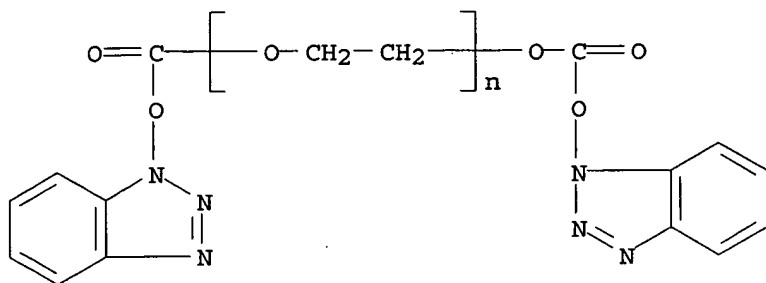
PAGE 2-A



RN 681286-88-4 HCAPLUS
 CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, polymer
 with α -[(1H-benzotriazol-1-yloxy)carbonyl]- ω -[(1H-
 benzotriazol-1-yloxy)carbonyl]oxy]poly(oxy-1,2-ethanediyl) (9CI) (CA
 INDEX NAME)

CM 1

CRN 178676-34-1
 CMF (C2 H4 O)n C14 H8 N6 O5
 CCI PMS



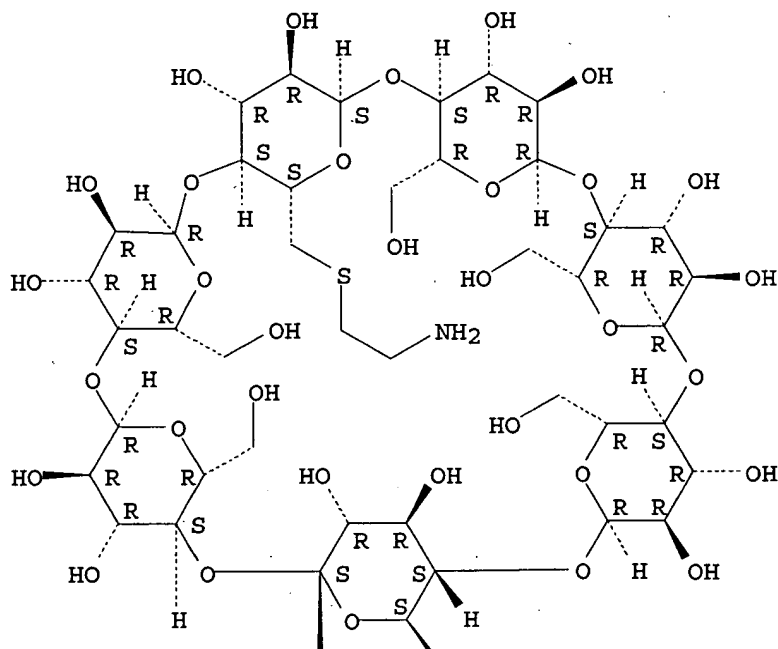
CM 2

CRN 101652-40-8

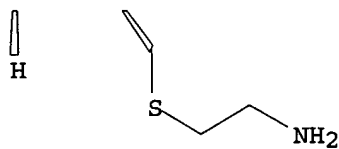
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



L55 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2004:220231 HCAPLUS
 DOCUMENT NUMBER: 140:276173
 TITLE: Cyclodextrin-based **polymers** for therapeutics delivery
 INVENTOR(S): Cheng, Jianjun; Davis, Mark E.; Khin, Kay T.
 PATENT ASSIGNEE(S): Insert Therapeutics, Inc., USA
 SOURCE: PCT Int. Appl., 159 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022099	A2	20040318	WO 2003-US27588	20030904
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004077595	A1	20040422	US 2003-656838	20030905
PRIORITY APPLN. INFO.:			US 2002-408855P	P 20020906
			US 2002-422830P	P 20021031
			US 2003-451998P	P 20030304

AB The present invention relates to novel compns. of therapeutic cyclodextrin-containing **polymeric** compds. designed as a carrier for delivery of small mol. therapeutics and pharmaceutical compns. thereof. These cyclodextrin-containing **polymers** improve drug stability and solubility, and reduce toxicity of the small mol. therapeutics when used in vivo. Furthermore, by selecting from a variety of linker groups and targeting ligands the **polymers** present methods for controlled delivery of the therapeutic agents. The invention also relates to methods of treating subjects with the therapeutic compns. described herein. The invention further relates to methods for conducting pharmaceutical business comprising manufacturing, licensing, or distribution kits containing

or relating to the **polymeric** compds. described herein.

IC ICM A61K047-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 35

ST cyclodextrin **polymer** carrier drug delivery; controlled drug delivery cyclodextrin **polymer** carrier

IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (agonists and antagonists; cyclodextrin-based **polymer** carriers for therapeutics delivery)

IT Drug delivery systems

(carriers; cyclodextrin-based **polymer** carriers for therapeutics delivery)

IT Drug delivery systems

(controlled-release; cyclodextrin-based **polymer** carriers for

- therapeutics delivery)
- IT Antitumor agents
(cyclodextrin-based **polymer** carriers for therapeutics delivery)
- IT Drug delivery systems
(kits; cyclodextrin-based **polymer** carriers for therapeutics delivery)
- IT Polyoxyalkylenes, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cyclodextrin-based **polymer** carriers for therapeutics delivery)
- IT Peptides, biological studies
Polymers, biological studies
Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic; cyclodextrin-based **polymer** carriers for therapeutics delivery)
- IT 152310-58-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(crosslinking agent; preparation of cyclodextrin-based **polymer** carriers for therapeutics delivery)
- IT 204133-74-4DP, conjugates with ethoxylated polycyclodextrins
362496-98-8DP, conjugates with ethoxylated polycyclodextrins
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclodextrin-based **polymer** carriers for therapeutics delivery)
- IT 672333-68-5P
RL: PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyclodextrin-based **polymer** carriers for therapeutics delivery)
- IT 672333-68-5DP, amides with glycine camptothecin ester
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclodextrin-based **polymer** carriers for therapeutics delivery)
- IT 7689-03-4, Camptothecin
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(preparation of cyclodextrin-based **polymer** carriers for therapeutics delivery)
- IT 204133-74-4P 362496-98-8P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyclodextrin-based **polymer** carriers for therapeutics delivery)
- IT 52-90-4, L-Cysteine, reactions 56-89-3, Cystine, reactions 60-23-1, Cysteamine 68-11-1, Mercaptoacetic acid, reactions 98-59-9, Tosyl chloride 405-39-0 677-24-7, Methyl dichlorophosphate 768-94-5, 1-Aminoadamantane 929-59-9 1155-64-2 1676-73-9 3406-84-6, Biphenyl-4,4'-disulfonyl chloride 4530-20-5 6066-82-6, N-Hydroxysuccinimide 6240-11-5, 1-Adamantane ethanol 7585-39-9, β -Cyclodextrin 9002-98-6, PEI 10389-65-8 17768-41-1, 1-Adamantane methylamine 21160-83-8 23911-25-3, Ethylenediamine tetraacetic dianhydride 23911-26-4, Diethylenetriamine pentaacetic dianhydride 25322-68-3, Polyethylene glycol 28320-73-2 29390-67-8

51974-68-6, Sodium 2-aminoethylthiolate 488085-18-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of cyclodextrin-based **polymer** carriers for therapeutics delivery)

IT 108-30-5P, Succinic anhydride, preparation 16352-26-4P 29390-66-7P,
6-Iodo β -Cyclodextrin 67217-55-4P, β -Cyclodextrin 6-tosylate
73499-21-5P 73667-73-9P 76700-72-6P 85419-94-9P
101652-40-8P 120527-66-4DP, cyclodextrinamide derivs.,
camptothecin conjugates 153445-05-7P 204133-72-2P 362496-95-5P
614744-04-6P 614744-05-7P 614744-06-8P
614744-08-0P 614744-10-4P 672333-40-3P
672333-43-6P 672333-45-8P 672333-47-0P 672333-50-5P
672333-51-6P 672333-52-7P 672333-53-8P 672333-54-9P
672333-55-0P 672333-57-2P 672333-60-7P
672333-61-8P 672333-64-1P 672333-65-2P
672333-69-6P 672333-70-9P 672333-72-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(preparation of cyclodextrin-based **polymer** carriers for therapeutics delivery)

IT 1397-89-3DP, Amphotericin B, conjugates with ethoxylated polycyclodextrins
9002-98-6DP, cyclodextrin derivs., camptothecin conjugates 25513-46-6DP,
cyclodextrinamide derivs., camptothecin conjugates 29390-67-8DP,
reaction products with polyphosphoesters, camptothecin conjugates
106973-21-1DP, cyclodextrinamide derivs., camptothecin conjugates
176669-13-9DP, reaction products with polyglutamic acid, cyclodextrinamide
derivs. 204133-36-8DP, conjugates with ethoxylated polycyclodextrins
215604-12-9DP, conjugates with ethoxylated polycyclodextrins
362496-97-7DP, reaction products with ethylene-maleic anhydride
polymers, cyclodextrinamide derivs. 672333-53-8DP, conjugates
with ethoxylated polycyclodextrins 672333-55-0DP, conjugates with
glycine camptothecin ester 672333-57-2DP, conjugates with glycine
camptothecin ester 672333-60-7DP, conjugates with glycine camptothecin
ester 672333-61-8DP, conjugates with glycine camptothecin ester
672333-62-9P 672333-65-2DP, amides with N-(3-carboxyl-1-
oxopropyl)glycine camptothecin ester 672333-66-3P 672333-67-4P
672333-69-6DP, **polymers** with cyclodextrinamide derivs.,
camptothecin conjugates 672333-71-0P 672913-15-4DP, amides with
glycine camptothecin ester and NHS folate derivative 672932-77-3DP,
camptothecin conjugates 672932-77-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of cyclodextrin-based **polymer** carriers for therapeutics delivery)

IT 672333-68-5P

RL: PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(preparation of cyclodextrin-based **polymer** carriers for therapeutics delivery)

RN 672333-68-5 HCAPLUS

CN L-Cysteine, S,S'-(6A,6D-dideoxy- β -cyclodextrin-6A,6D-diyl)bis-,
polymer with α -(3-carboxy-1-oxopropyl)- ω -(3-carboxy-1-
oxopropoxy)poly(oxy-1,2-ethanediy) (9CI) (CA INDEX NAME)

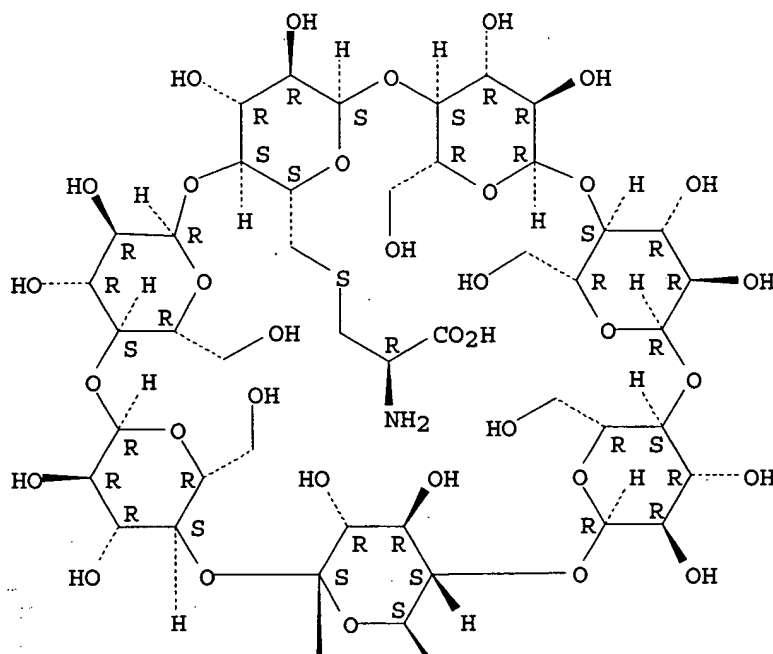
CM 1

CRN 614744-04-6

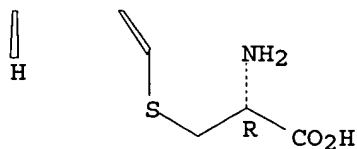
CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

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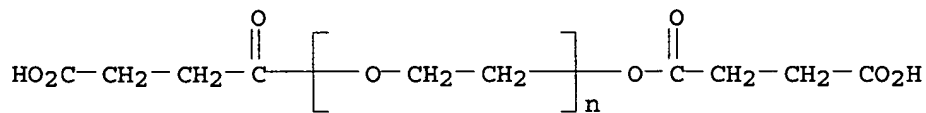


CM 2

CRN 37684-51-8

CMF (C2 H4 O)_n C8 H10 O7

CCI PMS



IT 76700-72-6P 101652-40-8P 614744-04-6P
 614744-05-7P 614744-06-8P 614744-08-0P
 614744-10-4P 672333-40-3P 672333-43-6P
 672333-45-8P 672333-55-0P 672333-57-2P

672333-61-8P 672333-64-1P 672333-65-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

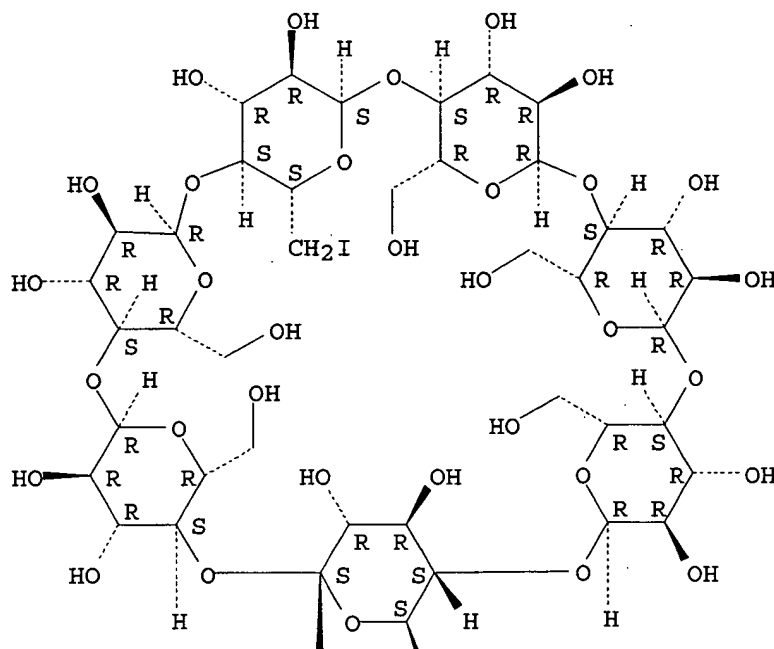
(preparation of cyclodextrin-based polymer carriers for therapeutics delivery)

RN 76700-72-6 HCAPLUS

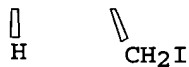
CN β -Cyclodextrin, 6A,6D-dideoxy-6A,6D-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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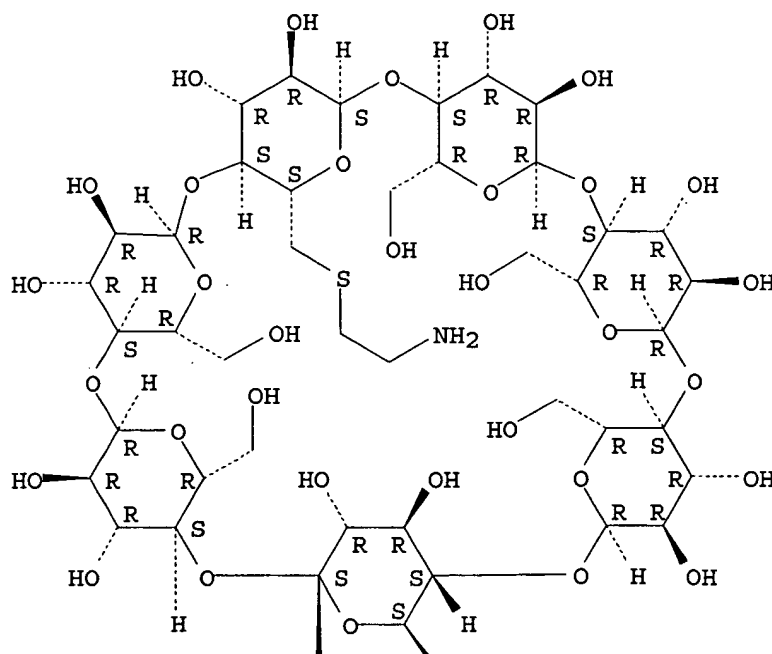


RN 101652-40-8 HCAPLUS

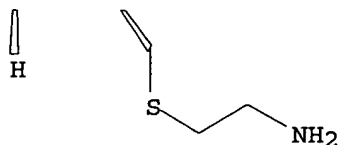
CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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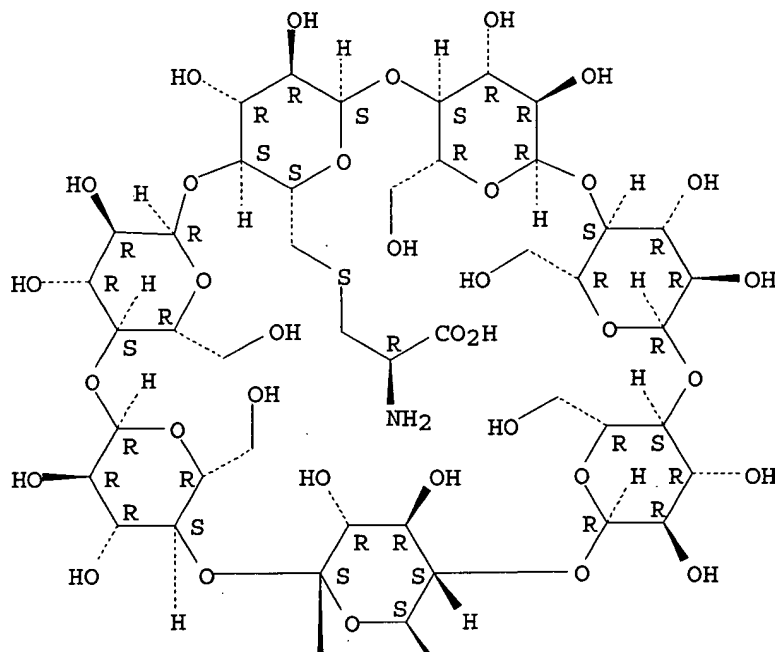


RN 614744-04-6 HCAPLUS

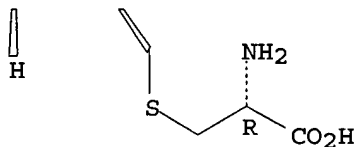
CN L-Cysteine, S,S'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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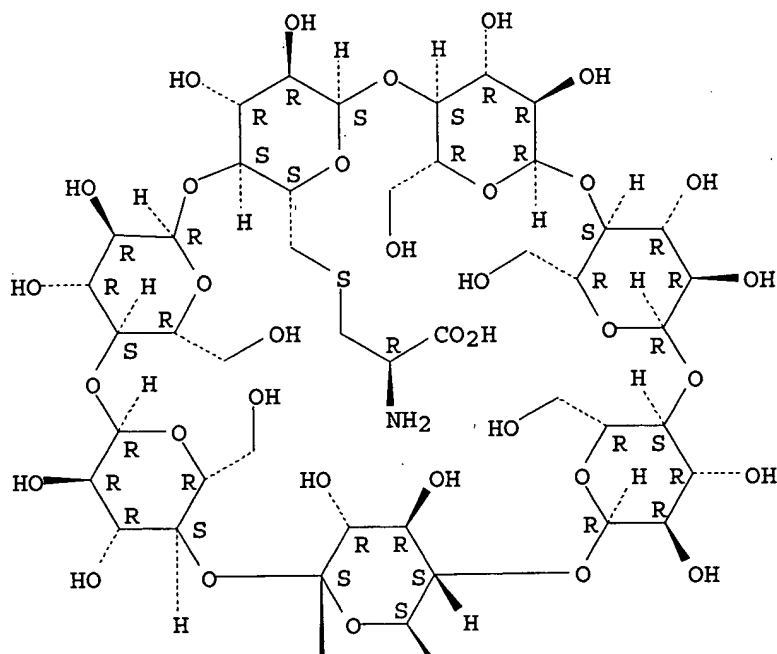
RN 614744-05-7 HCAPLUS
 CN L-Cysteine, S,S'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis-,
 polymer with α-[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]-
 ω-[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropoxy]poly(oxy-1,2-
 ethanediyl) (9CI) (CA INDEX NAME)

CM 1

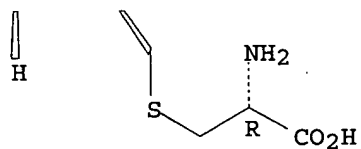
CRN 614744-04-6
 CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

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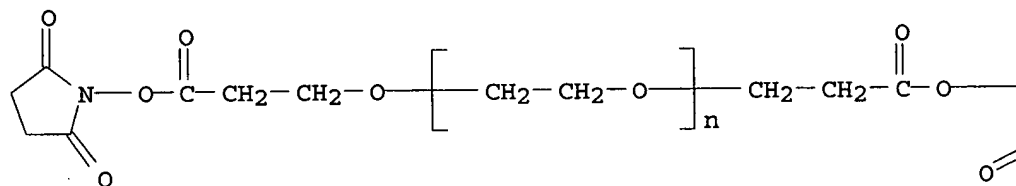
CM 2

CRN 123502-57-8

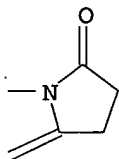
CMF (C2 H4 O)_n C14 H16 N2 O9

CCI PMS

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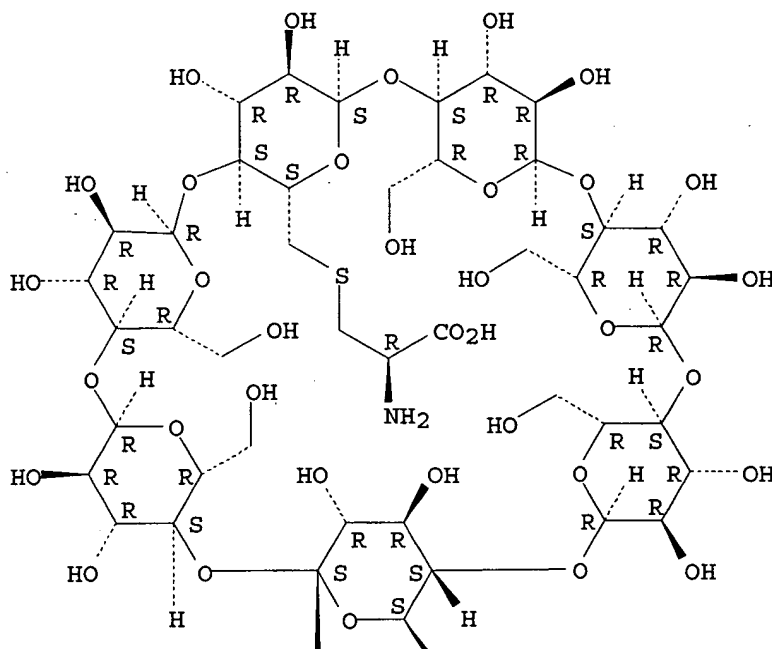
RN 614744-06-8 HCAPLUS
 CN L-Cysteine, S,S'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis-,
 polymer with α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutyl]-
 ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]poly(oxy-1,2-
 ethanediyl) (9CI) (CA INDEX NAME)

CM 1

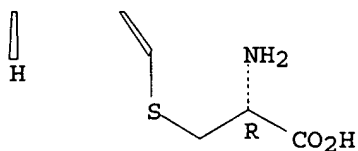
CRN 614744-04-6
 CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

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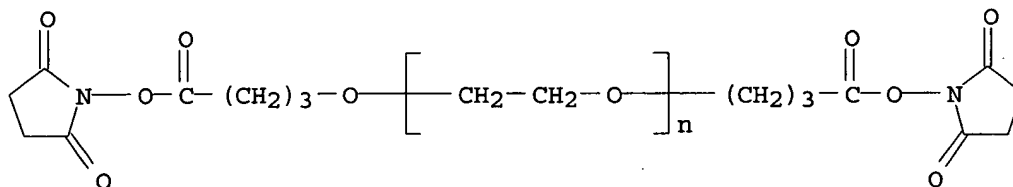


CM 2

CRN 159194-63-5

CMF (C2 H4 O)_n C16 H20 N2 O9

CCI PMS



RN 614744-08-0 HCAPLUS

CN L-Cysteine, S,S'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis-,
 polymer with α-[(1H-benzotriazol-1-yloxy)carbonyl]-ω-[[[(1H-
 benzotriazol-1-yloxy)carbonyl]oxy]poly(oxy-1,2-ethanediyl) (9CI) (CA
 INDEX NAME)

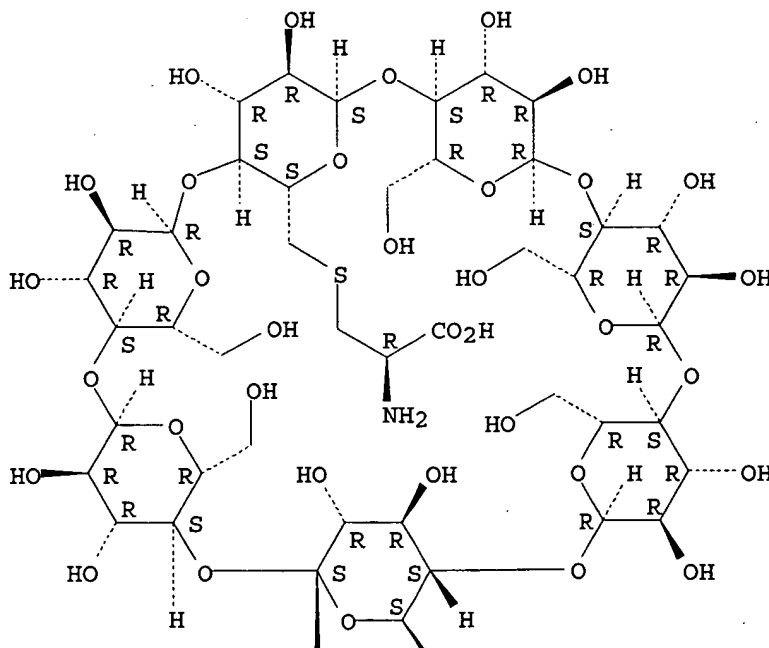
CM 1

CRN 614744-04-6

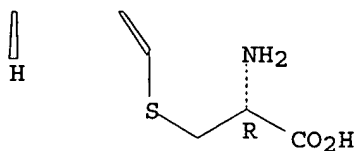
CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

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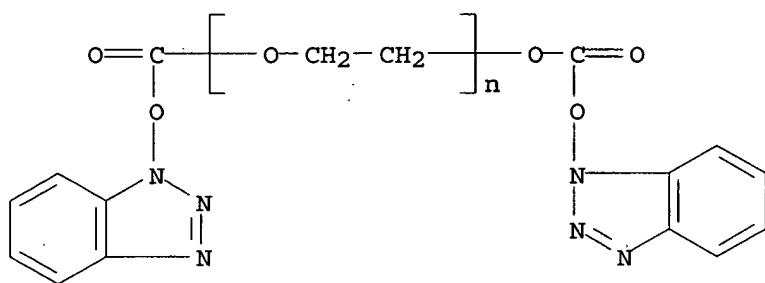


CM 2

CRN 178676-34-1

CMF (C2 H4 O)_n C14 H8 N6 O5

CCI PMS



RN 614744-10-4 HCAPLUS

CN L-Cysteine, S,S'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis-,
polymer with α-[(4-nitrophenoxy)carbonyl]-ω-[[4-nitrophenoxy)carbonyl]oxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

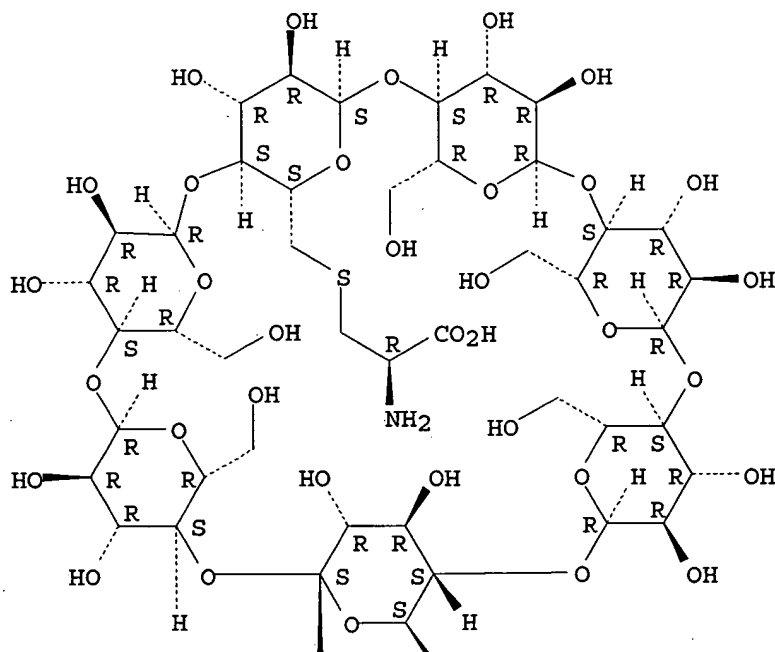
CM 1

CRN 614744-04-6

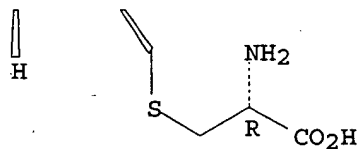
CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

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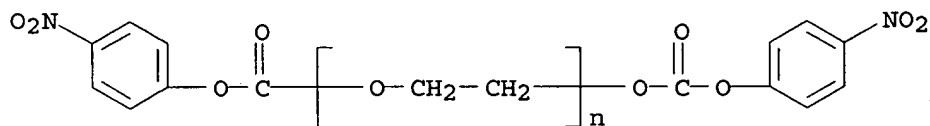


CM 2

CRN 150673-50-0

CMF (C2 H4 O)_n C14 H8 N2 O9

CCI PMS

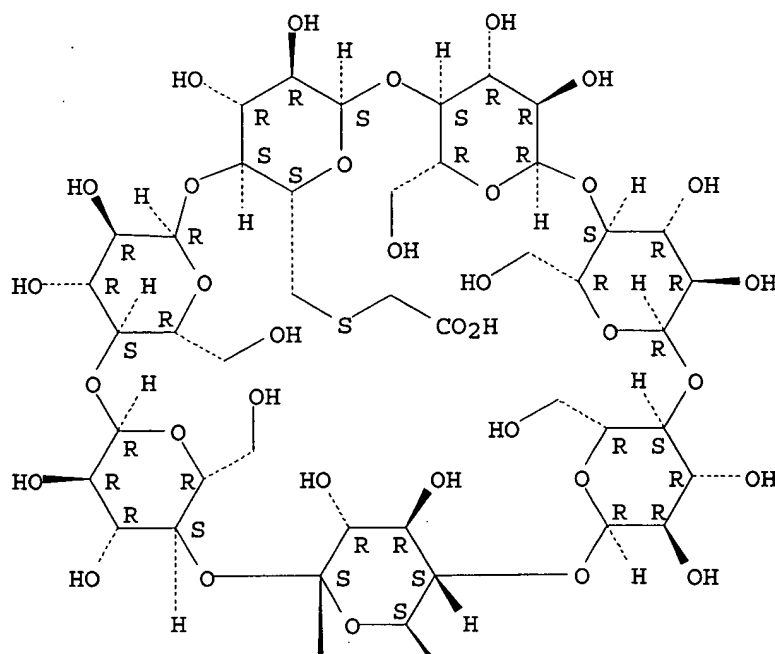


RN 672333-40-3 HCAPLUS

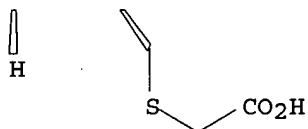
CN β-Cyclodextrin, 6A,6D-bis-S-(carboxymethyl)-6A,6D-dithio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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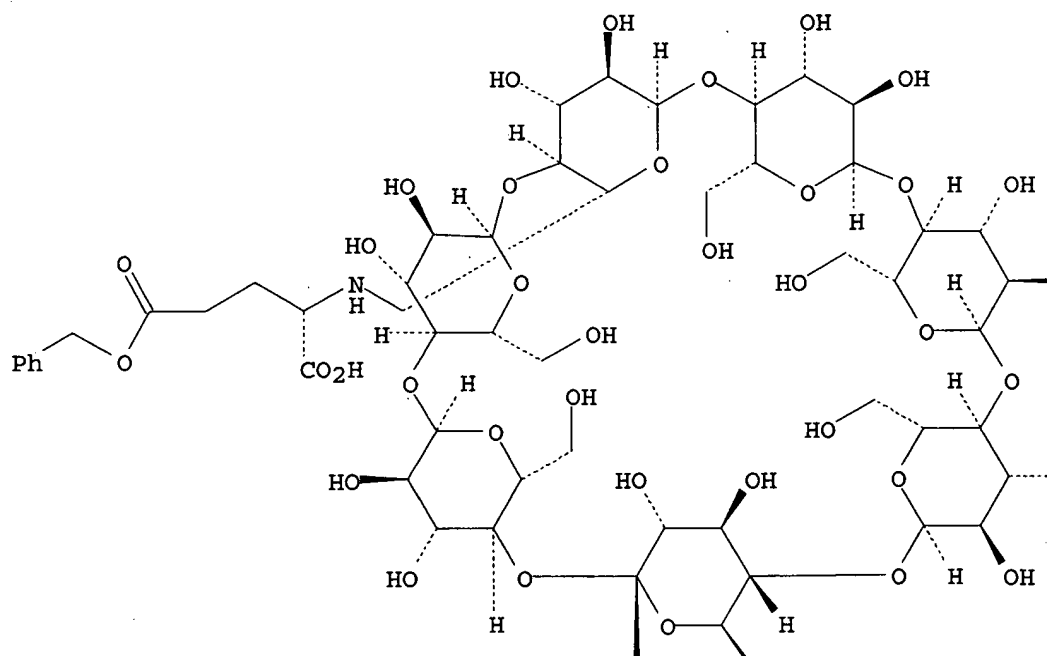


RN 672333-43-6 HCAPLUS

CN L-Glutamic acid, N,N'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis-,
5,5'-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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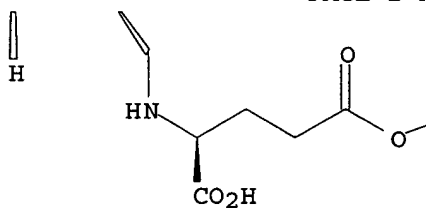


PAGE 1-B

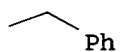
=OH

---OH

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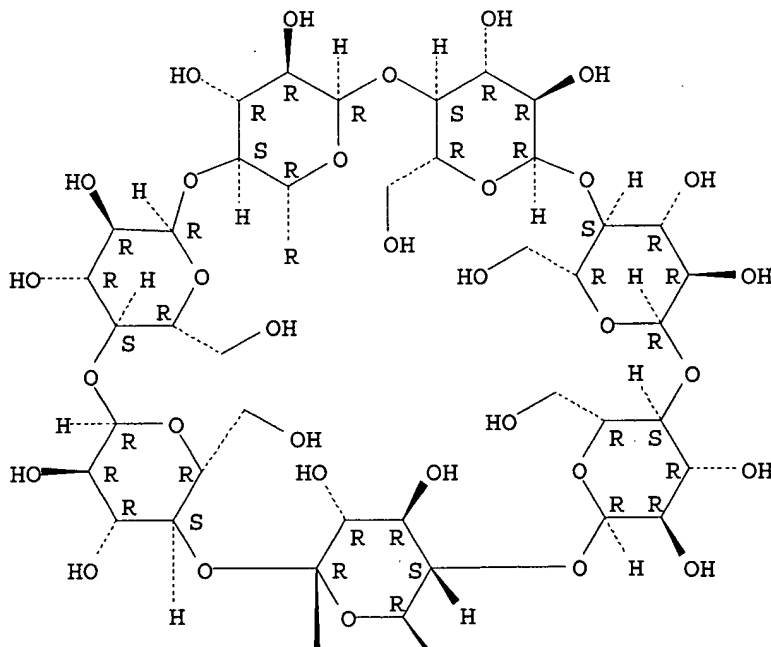


RN 672333-45-8 HCAPLUS

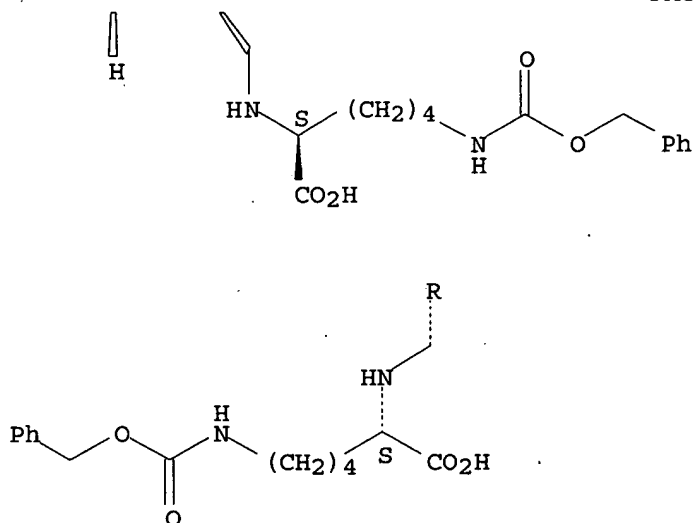
CN L-Lysine, N2,N2'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis[N6-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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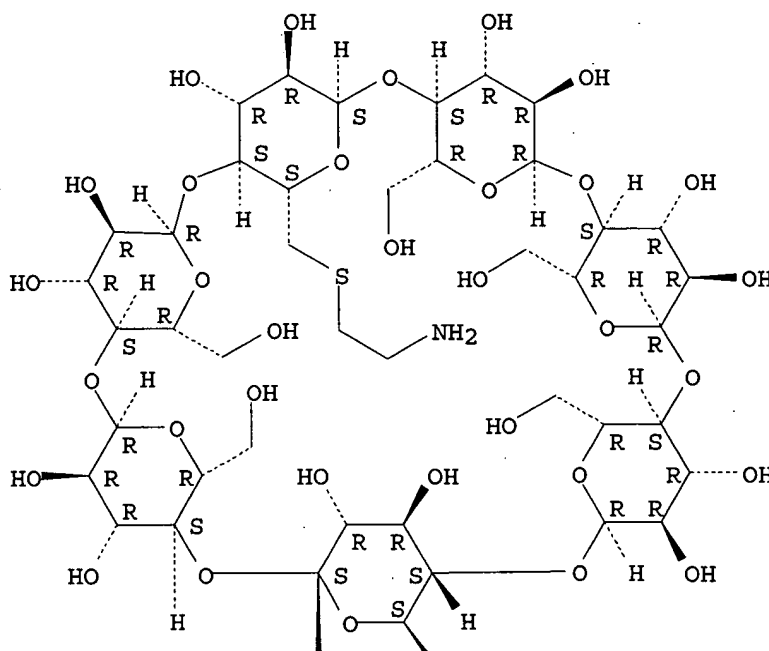
RN 672333-55-0 HCAPLUS
 CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, polymer
 with 4,4'-(1,2-ethanediyl)bis[2,6-morpholinedione] (9CI) (CA INDEX NAME)

CM 1

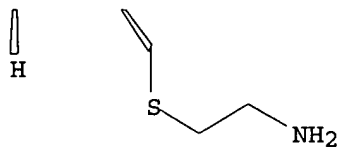
CRN 101652-40-8
 CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

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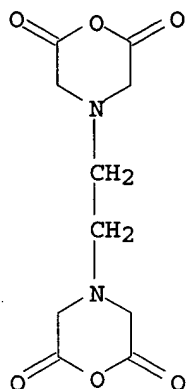
PAGE 2-A



CM 2

CRN 23911-25-3

CMF C10 H12 N2 O6



RN 672333-57-2 HCAPLUS

CN Glycine, N,N-bis[2-(2,6-dioxo-4-morpholinyl)ethyl]-, polymer with
6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio- β -cyclodextrin (9CI) (CA
INDEX NAME)

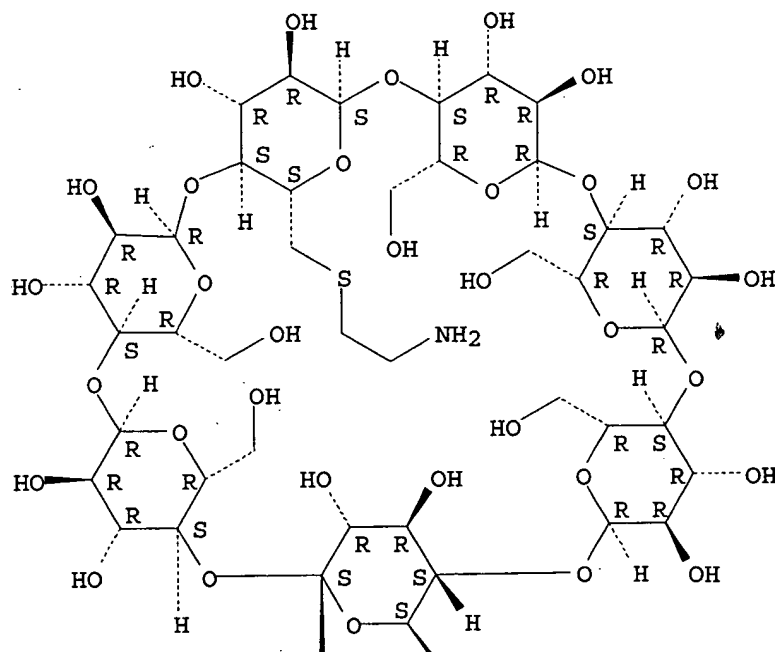
CM 1

CRN 101652-40-8

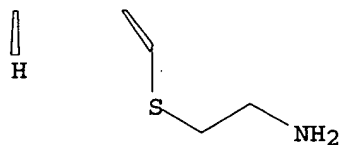
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

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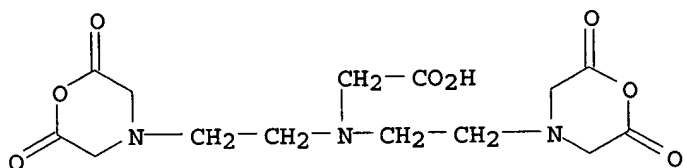
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CM 2

CRN 23911-26-4

CMF C14 H19 N3 O8



RN 672333-61-8 HCAPLUS

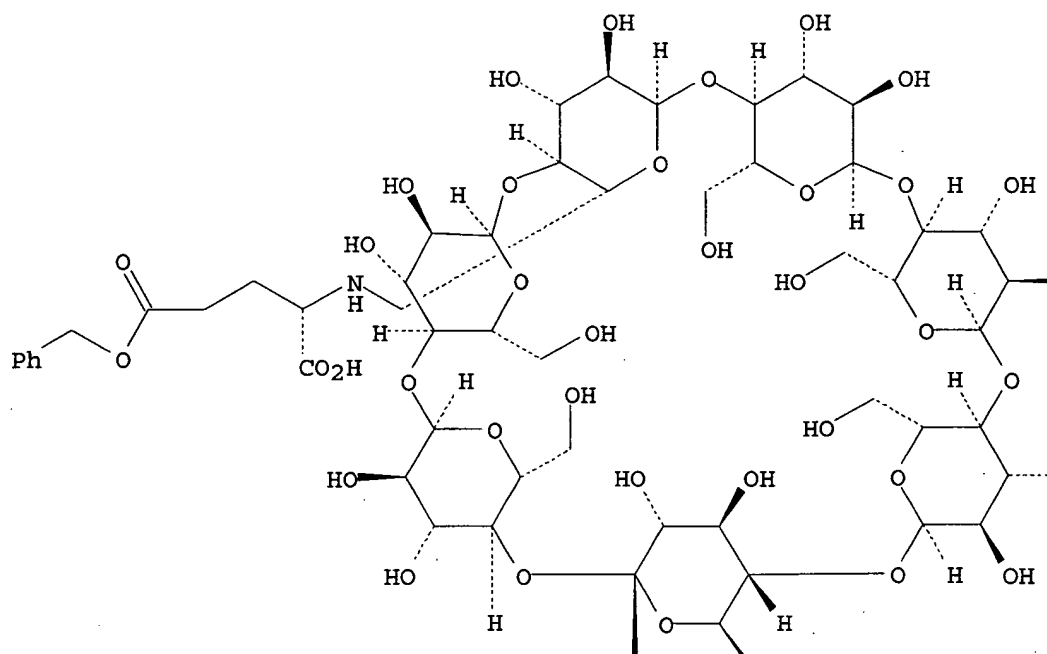
CN L-Glutamic acid, N,N'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis-,
5,5'-bis(phenylmethyl) ester, polymer with 2,2'-[1,2-ethanediylbis(oxy)]bis[ethanamine] (9CI) (CA INDEX NAME)

CM 1

CRN 672333-43-6
CMF C66 H96 N2 O41

Absolute stereochemistry.

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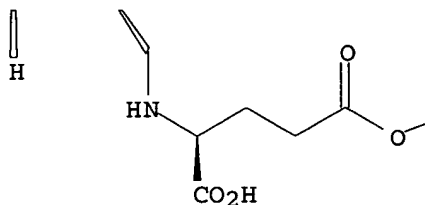


PAGE 1-B

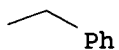
OH

OH

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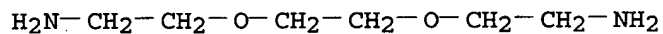
PAGE 2-B



CM 2

CRN 929-59-9

CMF C6 H16 N2 O2



RN 672333-64-1 HCAPLUS

CN L-Cystine, N,N'-bis[(1,1-dimethylethoxy)carbonyl]-, polymer with
6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-β-cyclodextrin (9CI) (CA
INDEX NAME)

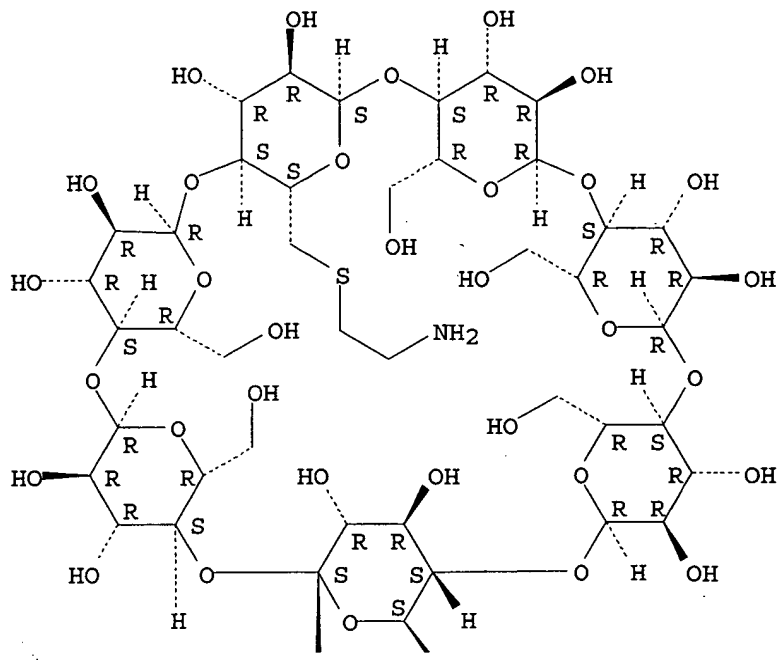
CM 1

CRN 101652-40-8

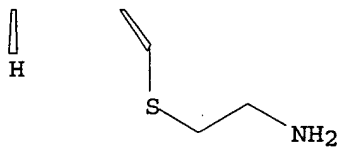
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

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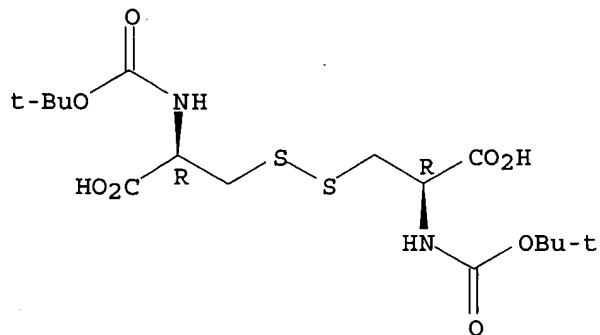


CM 2

CRN 10389-65-8

CMF C16 H28 N2 O8 S2

Absolute stereochemistry.



RN 672333-65-2 HCAPLUS
CN L-Cystine, polymer with 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio- β -cyclodextrin (9CI) (CA INDEX NAME)

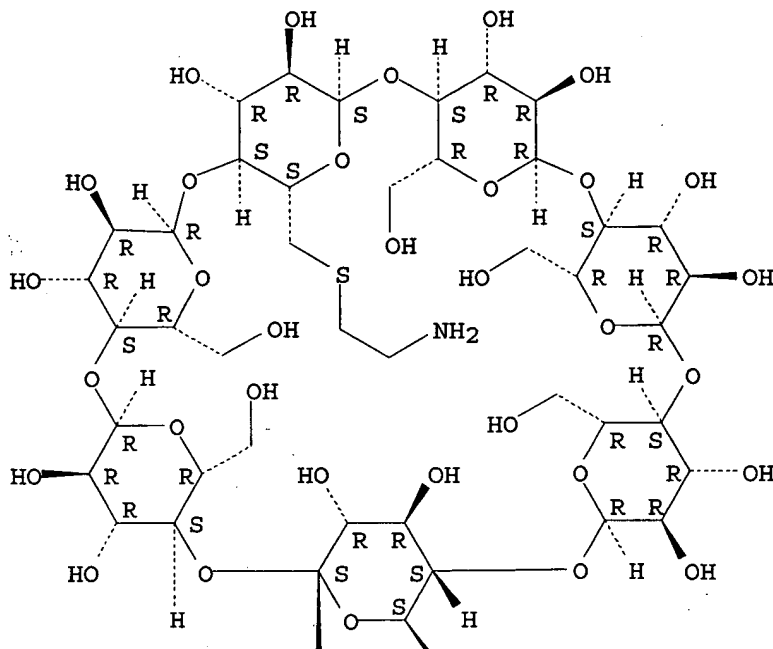
CM 1

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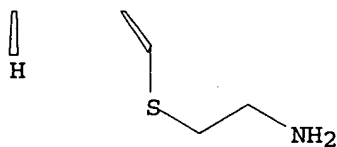
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

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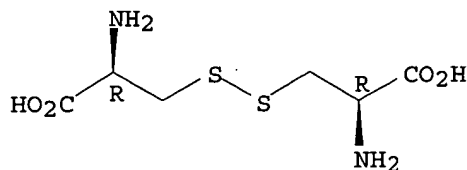


CM 2

CRN 56-89-3

CMF C6 H12 N2 O4 S2

Absolute stereochemistry.



L55 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:666072 HCAPLUS

DOCUMENT NUMBER: 139:328131

TITLE: Synthesis of Linear, β -Cyclodextrin-Based
Polymers and Their Camptothecin Conjugates

AUTHOR(S): Cheng, Jianjun; Khin, Kay T.; Jensen, Gregory S.; Liu,
Aijie; Davis, Mark E.

CORPORATE SOURCE: Insert Therapeutics, Inc., Pasadena, CA, 91107, USA

SOURCE: Bioconjugate Chemistry (2003), 14(5), 1007-1017

CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 6A,6D-Bis-(2-amino-2-carboxylethylthio)-6A,6D-dideoxy- β -cyclodextrin
1, a diamino acid derivative of β -cyclodextrin, is synthesized and
condensed with difunctionalized PEG comonomers to give linear, high mol.
weight (Mw over 50 kDa) β -cyclodextrin-based **polymers** (2-4)
with pendant functionality (carboxylate). 2-4 Are all highly soluble in
aqueous

solns. (over 200 mg/mL). 20-O-trifluoroglycinylcampthothecin, 5a, and
20-O-trifluoroglycinylglycinylglycinylcampthothecin, 5b, are synthesized
and conjugated to 2 to give **polymer**-campthothecin (CPT) prodrugs.
The solubility of CPT is increased by more than three orders of magnitude when
it is conjugated to 2. The rates of CPT release from the conjugates HGGG6
(high mol. weight **polymer** (Mw 97 kDa), glyglygly linker and 6 wt %
CPT loading) and HG6 (high MW **polymer** (Mw 97 kDa), gly linker
and 6 wt % CPT loading) in either mouse or human plasma are dramatically
accelerated over the rates of pure hydrolysis at pH = 7.4, indicating the
presence of enzymic cleavage as a rate-determining step at this pH in the
release of the CPT. The pH of aqueous solution has a large effect on

hydrolysis

rate of CPT from HGGG6 and HG6; the lower the pH, the slower the rate in
the range at $4.1 \leq \text{pH} \leq 13.1$. The IC₅₀'s of **polymer**
2e, CPT, and the CPT conjugates HG6 and HGGG6 are found to be cell-line
dependent with LS174T, HT29, A2780, and PC3 cells using in vitro MTT
assays. The parent **polymer** 2e has very low toxicity to all
cultured cells tested.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 35

ST camptothecin cyclodextrin PEG **copolymer** prodrug release

IT Human

(A2780 cell line; synthesis of linear, β -Cyclodextrin-based
polymers and their camptothecin conjugates)

IT Animal cell line

(HT-29; synthesis of linear, β -Cyclodextrin-based **polymers**
and their camptothecin conjugates)

IT Animal cell line

(LS174T; synthesis of linear, β -Cyclodextrin-based
polymers and their camptothecin conjugates)

IT Animal cell line

- (PC-3; synthesis of linear, β -Cyclodextrin-based **polymers** and their camptothecin conjugates)
- IT Polyoxyalkylenes, preparation
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(polyamide-; synthesis of linear, β -Cyclodextrin-based **polymers** and their camptothecin conjugates)
- IT Polyamides, preparation
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(polyoxyalkylene-; synthesis of linear, β -Cyclodextrin-based **polymers** and their camptothecin conjugates)
- IT Drug delivery systems
(prodrugs; synthesis of linear, β -Cyclodextrin-based **polymers** and their camptothecin conjugates)
- IT Antitumor agents
Dissolution
Hydrolysis
Stability
(synthesis of linear, β -Cyclodextrin-based **polymers** and their camptothecin conjugates)
- IT 204133-74-4DP, reaction products with cyclodextrin polyamides
362496-98-8DP, reaction products with cyclodextrin polyamides
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of linear, β -Cyclodextrin-based **polymers** and their camptothecin conjugates)
- IT 7689-03-4, 20(S)-Camptothecin
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(synthesis of linear, β -Cyclodextrin-based **polymers** and their camptothecin conjugates)
- IT 614744-05-7DP, camptothecin conjugate derivs. 614744-06-8P
614744-08-0P 614744-10-4P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of linear, β -Cyclodextrin-based **polymers** and their camptothecin conjugates)
- IT 52-90-4, L-Cysteine, reactions 4530-20-5 28320-73-2 34079-22-6
123502-57-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of linear, β -Cyclodextrin-based **polymers** and their camptothecin conjugates)
- IT 76700-72-6P 204133-74-4P 362496-98-8P 614744-04-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of linear, β -Cyclodextrin-based **polymers** and their camptothecin conjugates)
- IT 614744-05-7DP, camptothecin conjugate derivs. 614744-06-8P
614744-08-0P 614744-10-4P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of linear, β -Cyclodextrin-based **polymers** and their camptothecin conjugates)
- RN 614744-05-7 HCAPLUS
- CN L-Cysteine, S,S'-(6A,6D-dideoxy- β -cyclodextrin-6A,6D-diyl)bis-, polymer with α -[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]- ω -[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropoxy]poly(oxy-1,2-

ethanediyl) (9CI) (CA INDEX NAME)

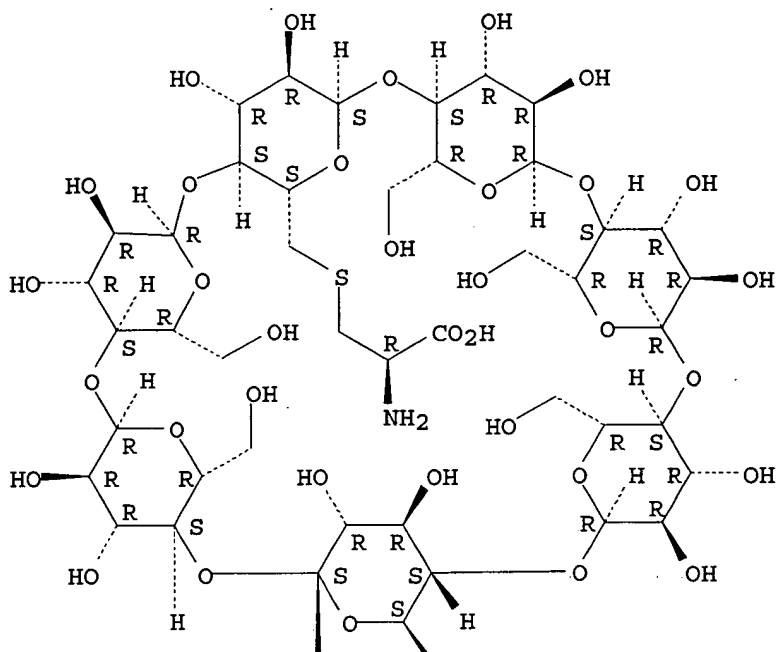
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CRN 614744-04-6

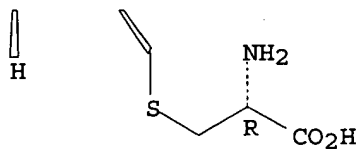
CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



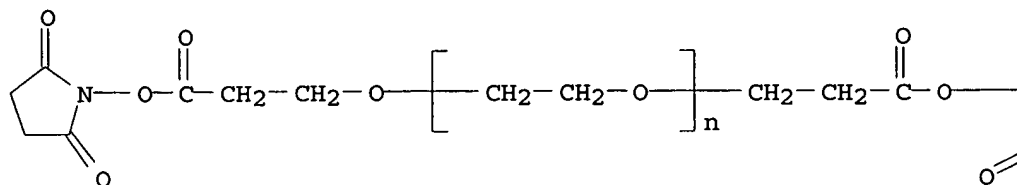
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CRN 123502-57-8

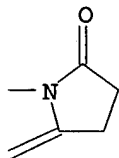
CMF (C2 H4 O)_n C14 H16 N2 O9

CCI PMS

PAGE 1-A



PAGE 1-B



RN 614744-06-8 HCAPLUS
 CN L-Cysteine, S,S'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis-,
 polymer with α-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutyl]-
 ω-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]poly(oxy-1,2-
 ethanediyl) (9CI) (CA INDEX NAME)

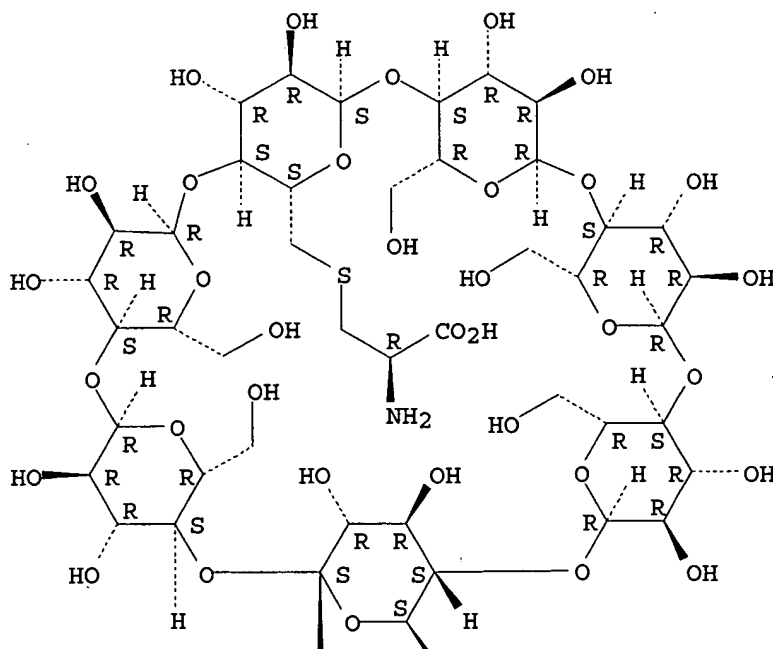
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CRN 614744-04-6

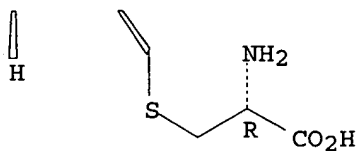
CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

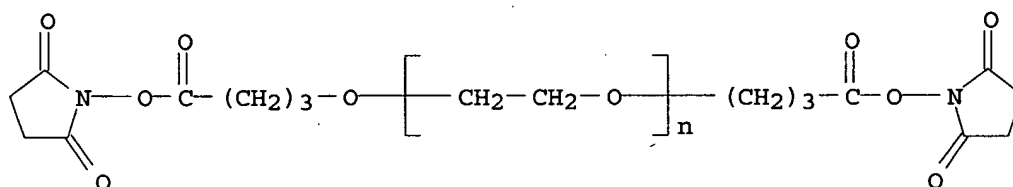


CM 2

CRN 159194-63-5

CMF (C2 H4 O)_n C16 H20 N2 O9

CCI PMS



RN 614744-08-0 HCAPLUS

CN L-Cysteine, S,S'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis-,
 polymer with α-[(1H-benzotriazol-1-yloxy)carbonyl]-ω-[[[(1H-
 benzotriazol-1-yloxy)carbonyl]oxy]poly(oxy-1,2-ethanediyl) (9CI) (CA
 INDEX NAME)

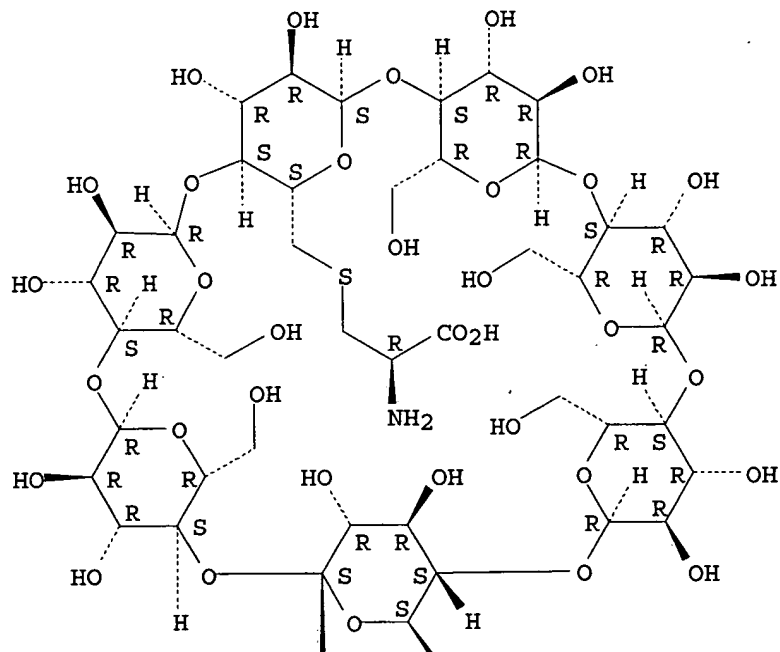
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CRN 614744-04-6

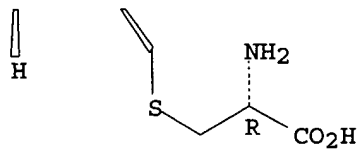
CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

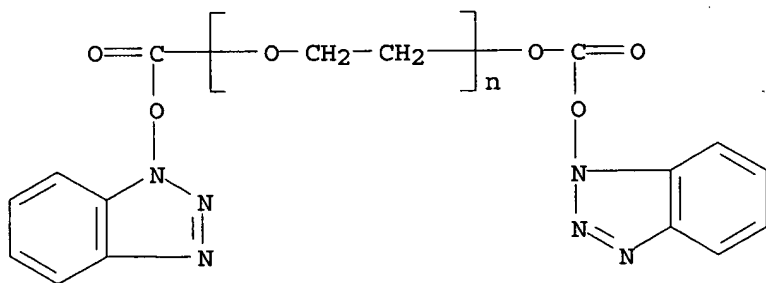


CM 2

CRN 178676-34-1

CMF (C2 H4 O)_n C14 H8 N6 O5

CCI PMS



RN 614744-10-4 HCAPLUS

CN L-Cysteine, S,S'-(6A,6D-dideoxy- β -cyclodextrin-6A,6D-diyl)bis-,
polymer with α -[(4-nitrophenoxy)carbonyl]- ω -[[[(4-nitrophenoxy)carbonyl]oxy]poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

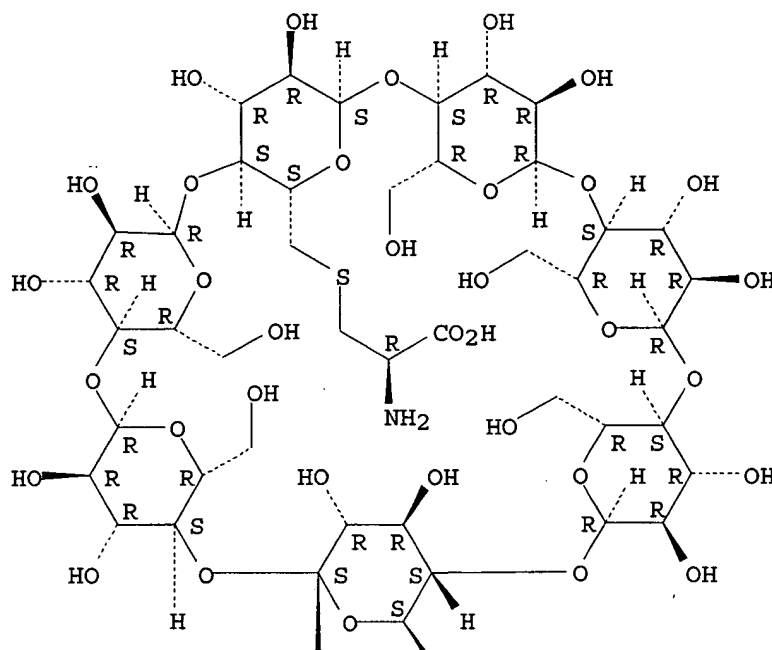
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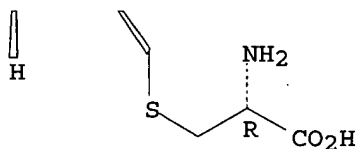
CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

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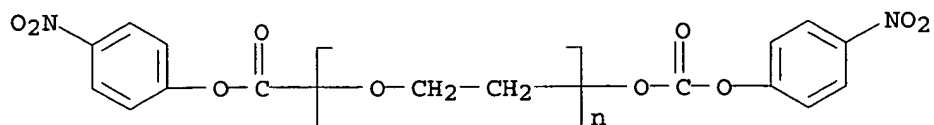


CM 2

CRN 150673-50-0

CMF (C2 H4 O)_n C14 H8 N2 O9

CCI PMS



IT 76700-72-6P 614744-04-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

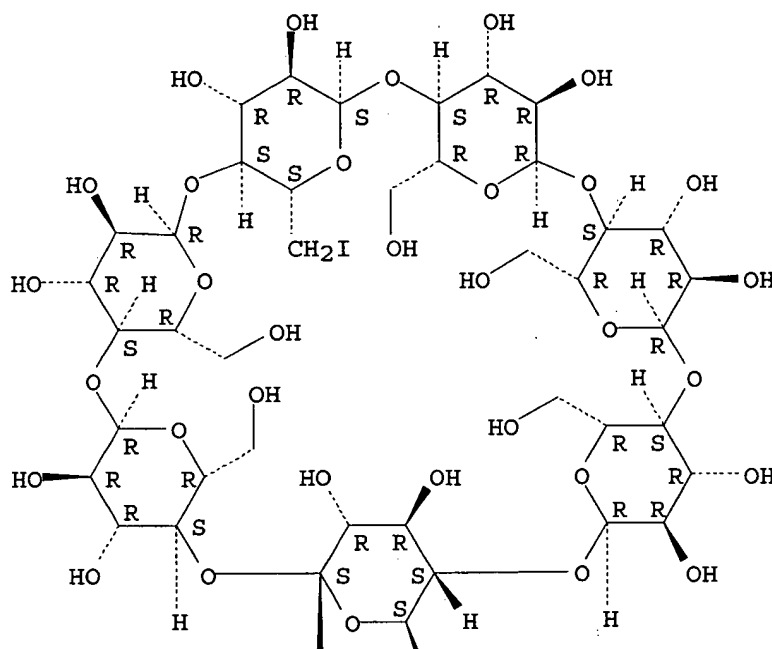
(synthesis of linear, β -Cyclodextrin-based polymers and their camptothecin conjugates)

RN 76700-72-6 HCAPLUS

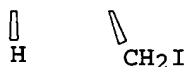
CN β -Cyclodextrin, 6A,6D-dideoxy-6A,6D-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

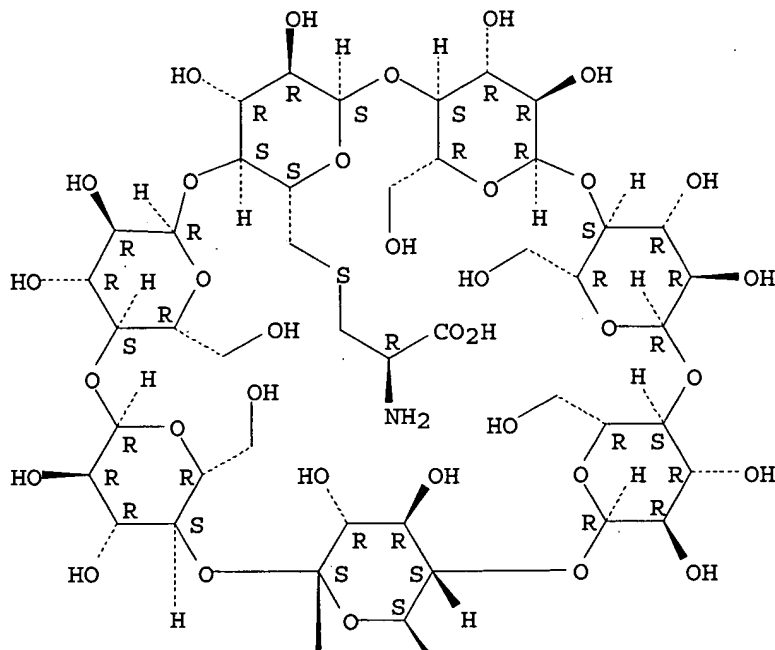


RN 614744-04-6 HCAPLUS

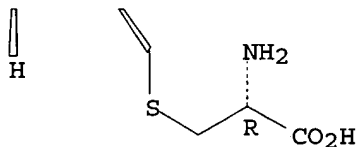
CN L-Cysteine, S,S'-(6A,6D-dideoxy- β -cyclodextrin-6A,6D-diyl)bis- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:965257 HCAPLUS

DOCUMENT NUMBER: 138:175678

TITLE: Structural Effects of Carbohydrate-Containing Polycations on Gene Delivery. 1. Carbohydrate Size and Its Distance from Charge Centers

AUTHOR(S): Reineke, Theresa M., Davis, Mark E.

CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA

SOURCE: Bioconjugate Chemistry (2003), 14(1), 247-254
CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cationic polymers have the ability to bind plasmid DNA (pDNA) through electrostatic interactions and condense it into particles that can be readily endocytosed by cultured cells. The effects that polycation

structure has on toxicity and gene delivery efficiency are investigated here by synthesizing a series of amidine-based polycations that contain the carbohydrates D-trehalose and β -cyclodextrin (CD) within the polycation backbone. The carbohydrate size (trehalose vs CD) and its distance from the charge centers affect the gene delivery behavior in BHK-21 cells. It is found that as the charge center is further removed from the carbohydrate unit, the toxicity is increased. Also, as the size of the carbohydrate moiety is enlarged from trehalose to β -cyclodextrin, the toxicity is reduced. The absence of a carbohydrate in the polycation produces high toxicity. All carbohydrate polycations transfect BHK-21 cells to approx. the same level of gene expression.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 33

IT 18729-73-2P 18933-88-5P 21100-03-8P 30923-00-3P 52290-50-3P
76700-72-6P 98126-99-9P 101652-40-8P

118308-81-9P 162825-08-3P 185613-13-2P 496932-11-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

(carbohydrate size and its distance from charge centers in relation to structural effects of carbohydrate-containing polycations on gene delivery)

IT 76700-72-6P 98126-99-9P 101652-40-8P
162825-08-3P 496932-11-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

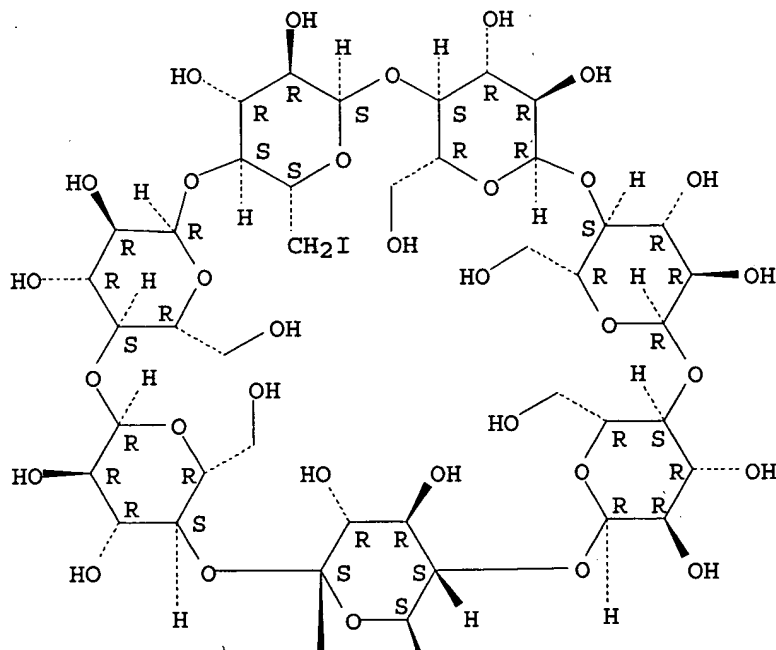
(carbohydrate size and its distance from charge centers in relation to structural effects of carbohydrate-containing polycations on gene delivery)

RN 76700-72-6 HCAPLUS

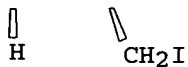
CN β -Cyclodextrin, 6A,6D-dideoxy-6A,6D-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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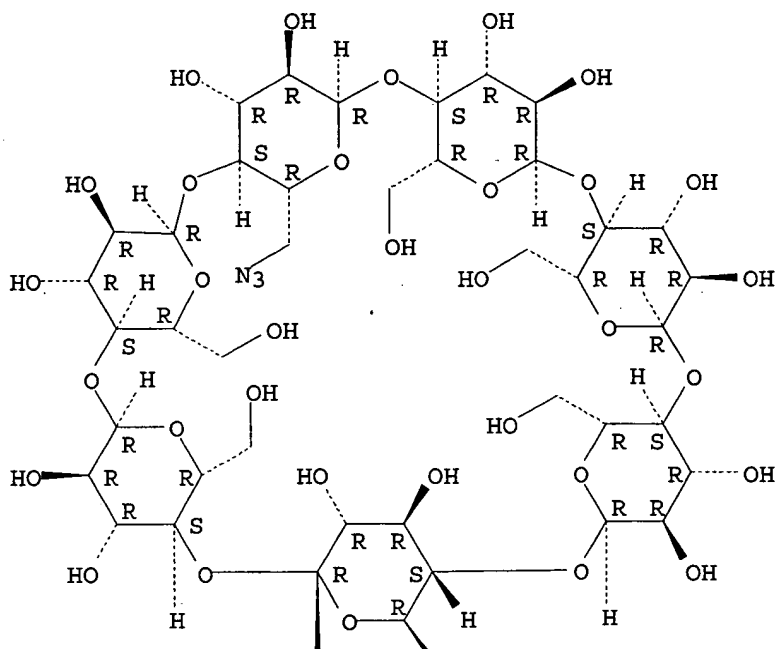


RN 98126-99-9 HCAPLUS

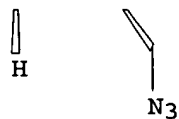
CN β-Cyclodextrin, 6A,6D-diazido-6A,6D-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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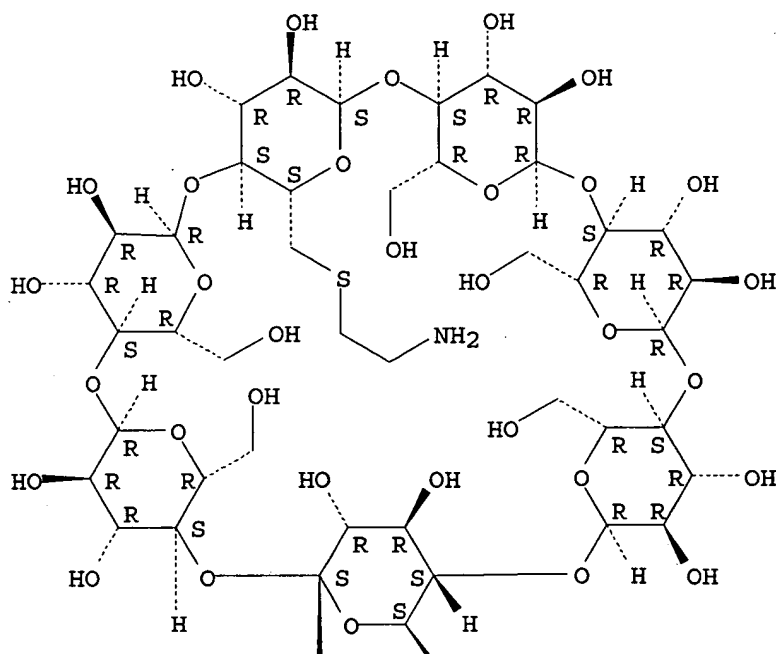


RN 101652-40-8 HCAPLUS

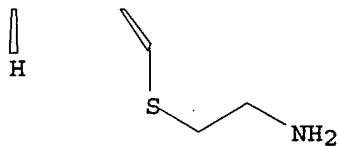
CN β-Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

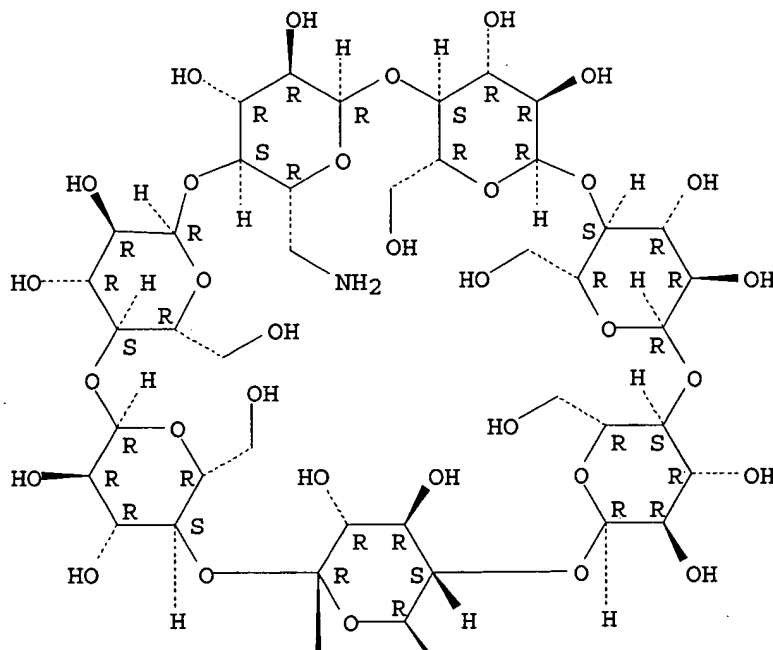


RN 162825-08-3 HCAPLUS

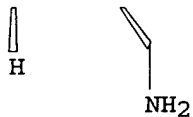
CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

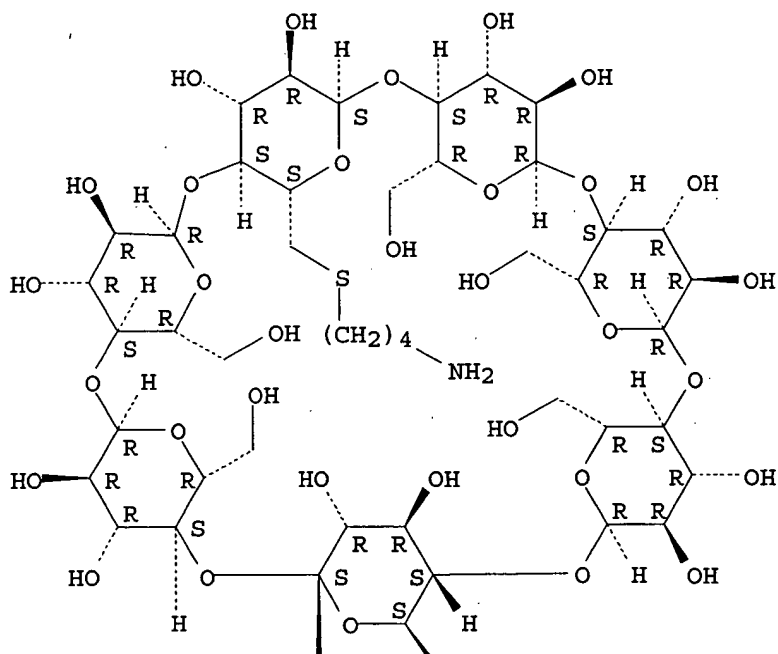


RN 496932-11-7 HCAPLUS

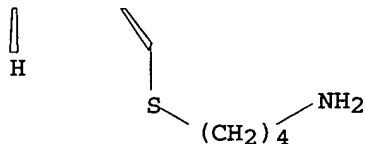
CN β -Cyclodextrin, 6A,6D-bis-S-(4-aminobutyl)-6A,6D-dithio- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:487421 HCAPLUS

DOCUMENT NUMBER: 137:47645

TITLE: Preparation of adamantyl-polyethylene glycol containing sugar and peptide residues and inclusion complexes as therapeutic agents

INVENTOR(S): Hwang, Pun Suzie; Gonzalez, Hector; Davis, Mark E.; Bellocq, Nathalie; Cheng, Jianjun

PATENT ASSIGNEE(S): California Institute of Technology, USA; Insert Therapeutics, Inc.

SOURCE: PCT Int. Appl., 138 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

 WO 2002049676 A2 20020627 WO 2001-US48620 20011219
 WO 2002049676 A3 20021227
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2002029065 A5 20020701 AU 2002-29065 20011219
 US 2003008818 A1 20030109 US 2001-21312 20011219
 US 2003017972 A1 20030123 US 2001-21294 20011219
 EP 1351710 A2 20031015 EP 2001-990201 20011219
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 PRIORITY APPLN. INFO.: US 2000-256341P P 20001219
 US 2000-256344P P 20001219
 US 2001-293543P P 20010529
 WO 2001-US48620 W 20011219

AB The invention provides a composition containing particulate composite of a **polymer** with a formula of adamantyl-(CH₂)_n-Ja-PEGx-Lb-(functional group)y wherein J is NH, C(O)NH(CH₂)_d, NHC(O)(CH₂)_d, XH₂SS, CO₂, (CH₂)_eOP(O)[O(CH₂)_e-adamantyl]O, peptide, polypeptide, NH(CO)CHR1NH(CO)CHR1NH; R1 is (CH₂)_aCO₂H, (CH₂)_aCONH₂; PEG is O(CH₂CH₂O)_z; where z is 2-500; L is H, NH₂, NH(CO)(CH₂)_e(CO)CH₂, SO₂CH:CH₂, SS, CO₂, carbohydrate residue; a is 0-1, b is 0-1; d is 0-6; e is 1-6; yr is 0-1, x is 0-1, and a therapeutic agent. The composition also contains a complexing agent. The **polymer** interacts with the complexing agent in a host-guest or a guest-host interaction to form an inclusion complex. A therapeutic composition of the invention may be used to deliver the therapeutic agent and to treat various disorders. Both the **polymer** of the particulate composite and the complexing agent may be used to introduce functionality into the therapeutic composition. The invention also relates to a method of preparing a composition. The method combines a therapeutic agent, a **polymer** having host or guest functionality, and a complexing agent having guest or host functionality to form the therapeutic composition. The complexing agent forms an inclusion complex with the **polymer**. The invention also relates to a method of delivering a therapeutic agent. According to the method, a therapeutically effective amount of a therapeutic composition of the invention is administered to a mammal (e.g. human or animal) in recognized need of the therapeutic.

IC ICM A61K047-48
 CC 35-8 (Chemistry of Synthetic High Polymers)
 Section cross-reference(s): 6, 33, 34, 63

IT Carbohydrates, preparation
 Glycols, preparation
 Peptides, preparation

Polymers, preparation

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
 USES (Uses)

(preparation of adamantylpolyethylene glycol containing sugar and peptide residues and inclusion complexes as therapeutic agents)

IT 57-88-5DP, Cholesterol, inclusion complexes 91-20-3DP, Naphthalene,
 inclusion complexes 281-23-2DP, Adamantane, inclusion complexes
 2292-79-7DP, inclusion complexes 26282-59-7DP, cyclodextrin thioethers

81644-55-5DP, polyethoxylated ether derivs. 107658-43-5DP,
adamantane-modified 254912-05-5P 254912-07-7P 254912-09-9P
264257-54-7DP, reaction products with polymeric cyclodextrin
thioamidoamides 275354-52-4P 275354-53-5DP, lactosylamine adducts
275354-54-6P 438490-85-8P 438490-87-0DP, adducts with lactose
438490-89-2DP, fluorescein derivs. 438490-89-2P 438490-90-5P
438490-95-0DP, human transferrin bound

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of adamantylpolyethylene glycol containing sugar and peptide
residues and inclusion complexes as therapeutic agents)

IT 63-42-3D, succinimidyl derivs. 118-31-0, 1-Naphthalenemethanamine
768-94-5, 1-Aminoadamantane 870-46-2, tert-Butyl carbazate 1676-73-9
3406-84-6 3416-24-8, Glucosamine 4942-47-6, Tricyclo[3.3.1.1^{3,7}]decane-
1-acetic acid 7535-00-4 7585-39-9, β -Cyclodextrin 14620-72-5
14641-93-1, α -Lactose 14651-42-4 17176-77-1, Dibenzyl phosphite
17768-41-1, Tricyclo[3.3.1.1^{3,7}]decane-1-methanamine 27072-45-3
32130-27-1 38285-78-8 39927-08-7 51974-68-6, Sodium
2-aminoethylthiolate 57757-57-0 58537-94-3 62087-82-5 67413-34-7
68528-80-3 123502-57-8 152310-58-2 155919-13-4 174569-25-6
254912-03-3 264257-54-7 275354-51-3 438490-88-1
438490-91-6 438490-94-9 438490-97-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of adamantylpolyethylene glycol containing sugar and peptide
residues and inclusion complexes as therapeutic agents)

IT 29390-66-7P 35625-91-3P 67217-55-4P 73499-21-5P 76700-72-6P
81644-55-5P 98126-99-9P 101652-40-8P 107658-43-5P
159790-69-9P 162825-08-3P 254912-04-4P
275354-53-5P 275354-55-7P 438490-86-9P 438490-87-0P
438490-92-7P 438490-93-8P 438490-95-0P 438490-96-1P 438490-98-3P
438490-99-4P 438491-00-0P 438491-01-1P 438491-02-2P 438491-03-3P
438491-04-4P 438491-05-5P 438491-06-6P 438491-07-7P 438491-08-8P
438491-09-9P 438491-10-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

(preparation of adamantylpolyethylene glycol containing sugar and peptide
residues and inclusion complexes as therapeutic agents)

IT 254912-03-3 275354-51-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of adamantylpolyethylene glycol containing sugar and peptide
residues and inclusion complexes as therapeutic agents)

RN 254912-03-3 HCAPLUS

CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2) (9CI)
(CA INDEX NAME)

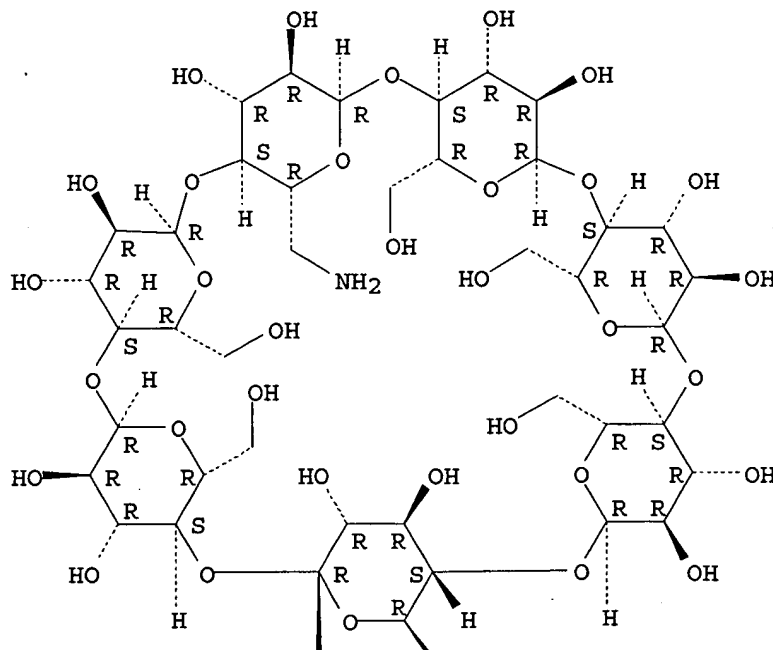
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CRN 162825-08-3

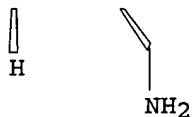
CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



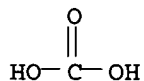
PAGE 2-A



CM 2

CRN 463-79-6

CMF C H2 O3



RN 275354-51-3 HCAPLUS

CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, carbonate (1:2) (salt) (9CI) (CA INDEX NAME)

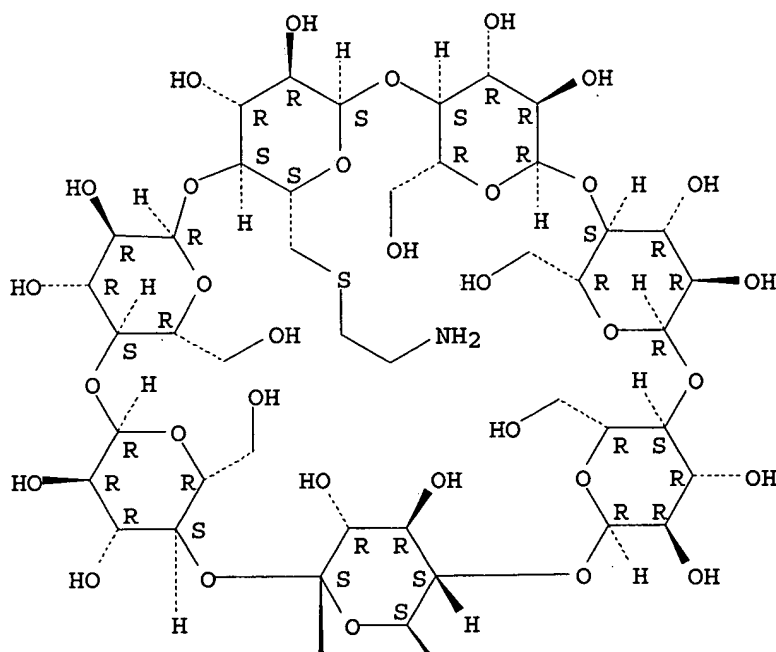
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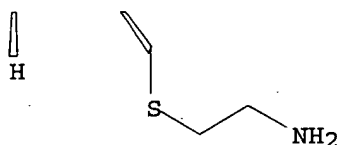
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

PAGE 1-A



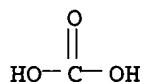
PAGE 2-A



CM 2

CRN 463-79-6

CMF C H2 O3



IT 76700-72-6P 98126-99-9P 101652-40-8P
 162825-08-3P 254912-04-4P 275354-53-5P
 275354-55-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)

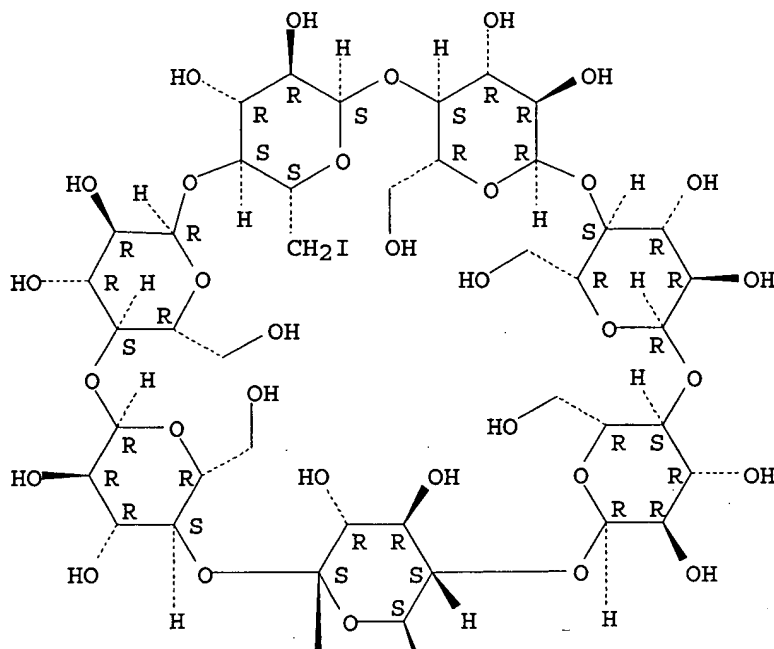
(preparation of adamantylpolyethylene glycol containing sugar and peptide
 residues and inclusion complexes as therapeutic agents)

RN 76700-72-6 HCAPLUS

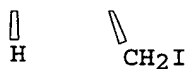
CN β -Cyclodextrin, 6A,6D-dideoxy-6A,6D-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

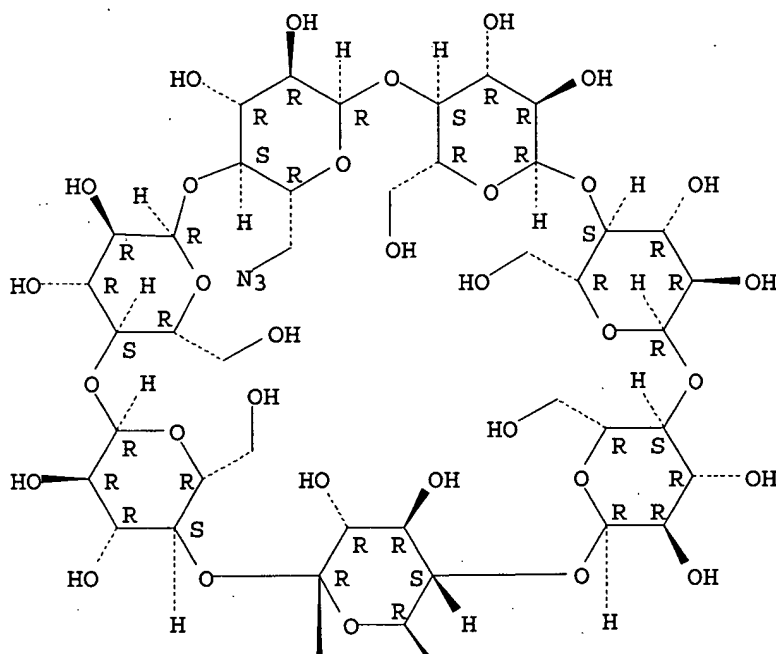


RN 98126-99-9 HCAPLUS

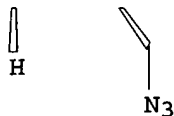
CN β -Cyclodextrin, 6A,6D-diazido-6A,6D-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



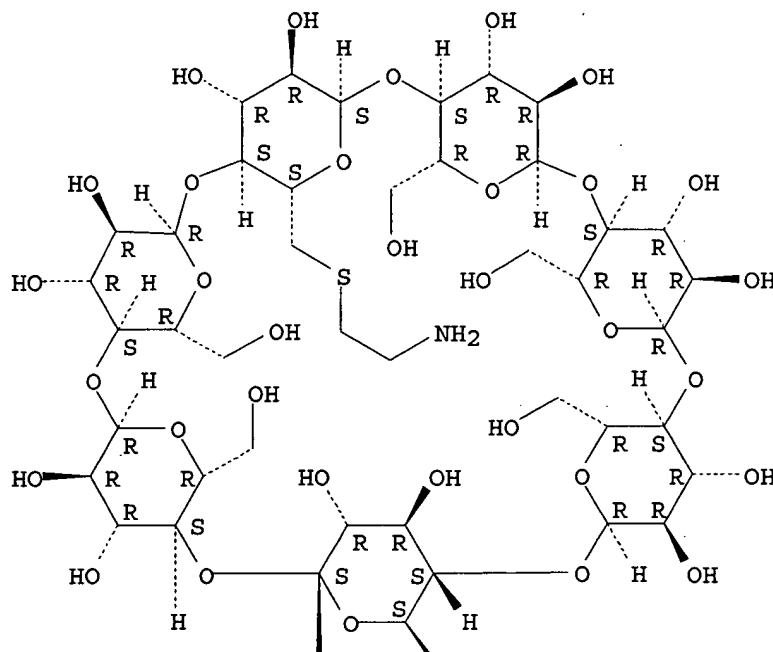
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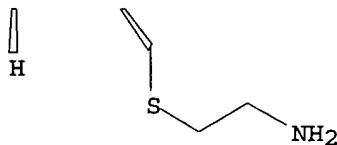
RN 101652-40-8 HCAPLUS
 CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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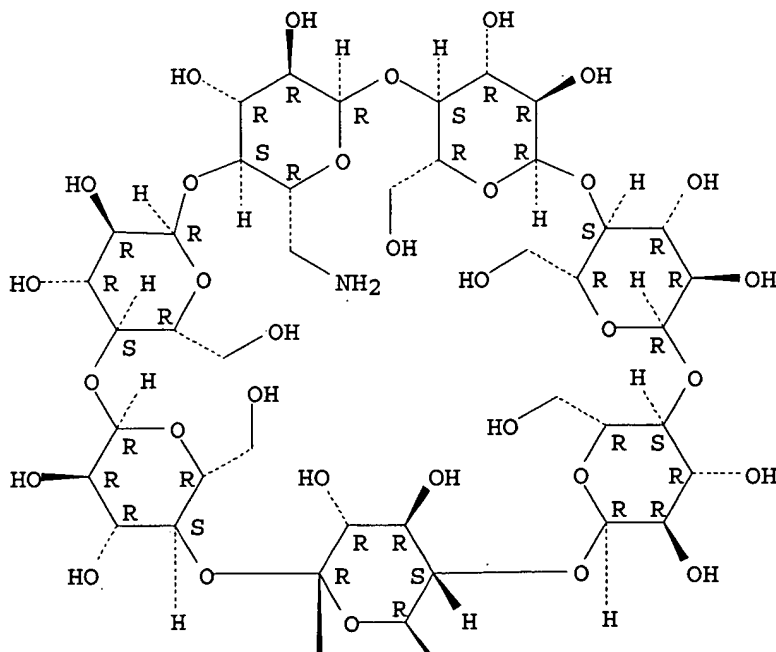


RN 162825-08-3 HCAPLUS

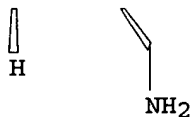
CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



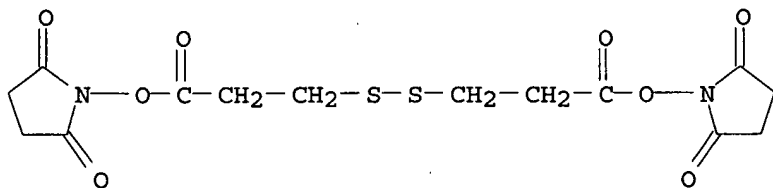
RN 254912-04-4 HCAPLUS

CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2),
polymer with 1,1'-[dithiobis[(1-oxo-3,1-propanediyl)oxy]]bis[2,5-
pyrrolidinedione] (9CI) (CA INDEX NAME)

CM 1

CRN 57757-57-0

CMF C14 H16 N2 O8 S2



CM 2

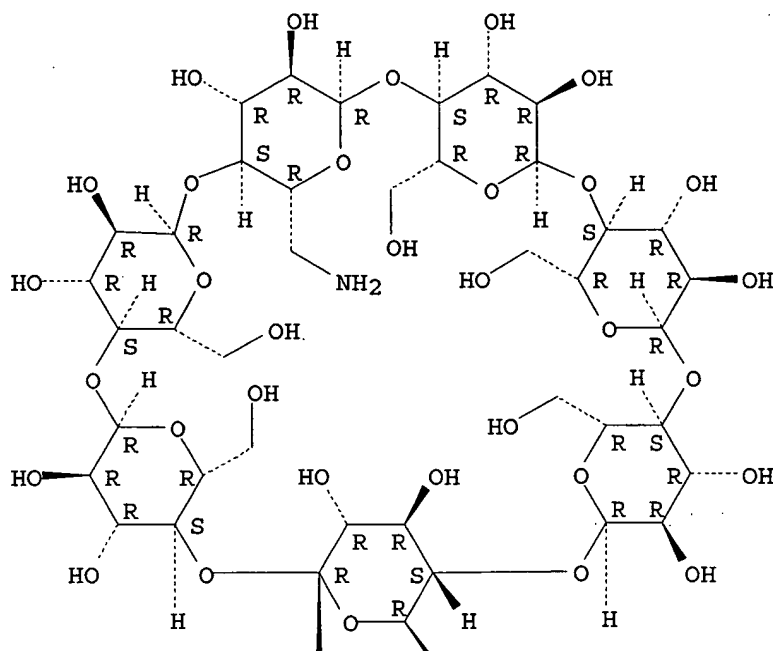
CRN 254912-03-3
 CMF C42 H72 N2 O33 . 2 C H2 O3

CM 3

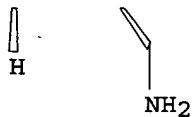
CRN 162825-08-3
 CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A

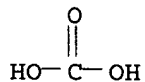


PAGE 2-A



CM 4

CRN 463-79-6
 CMF C H2 O3

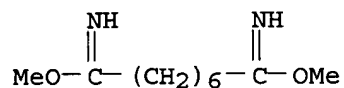


RN 275354-53-5 HCAPLUS
 CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, carbonate
 (1:2) (salt), polymer with dimethyl octanediimide dihydrochloride (9CI)
 (CA INDEX NAME)

CM 1

CRN 34490-86-3

CMF C10 H20 N2 O2 . 2 Cl H



●2 HCl

CM 2

CRN 275354-51-3

CMF C46 H80 N2 O33 S2 . 2 C H2 O3

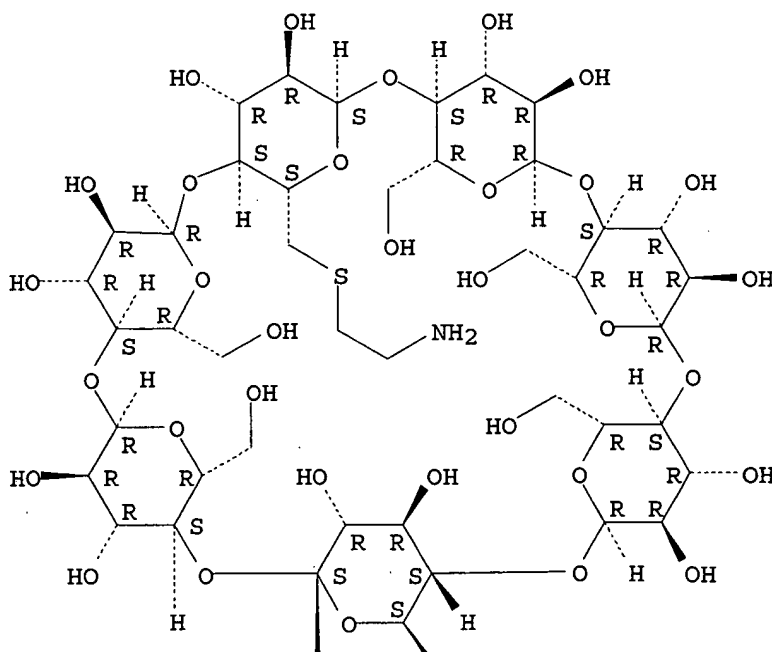
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CRN 101652-40-8

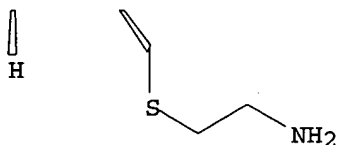
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

PAGE 1-A



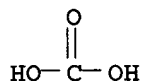
PAGE 2-A



CM 4

CRN 463-79-6

CMF C H2 O3



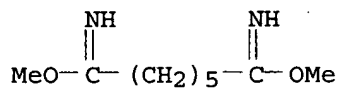
RN 275354-55-7 HCAPLUS

CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, carbonate
(1:2) (salt), polymer with dimethyl heptanediimide dihydrochloride (9CI)
(CA INDEX NAME)

CM 1

CRN 58537-94-3

CMF C9 H18 N2 O2 . 2 Cl H



● 2 HCl

CM 2

CRN 275354-51-3

CMF C46 H80 N2 O33 S2 . 2 C H2 O3

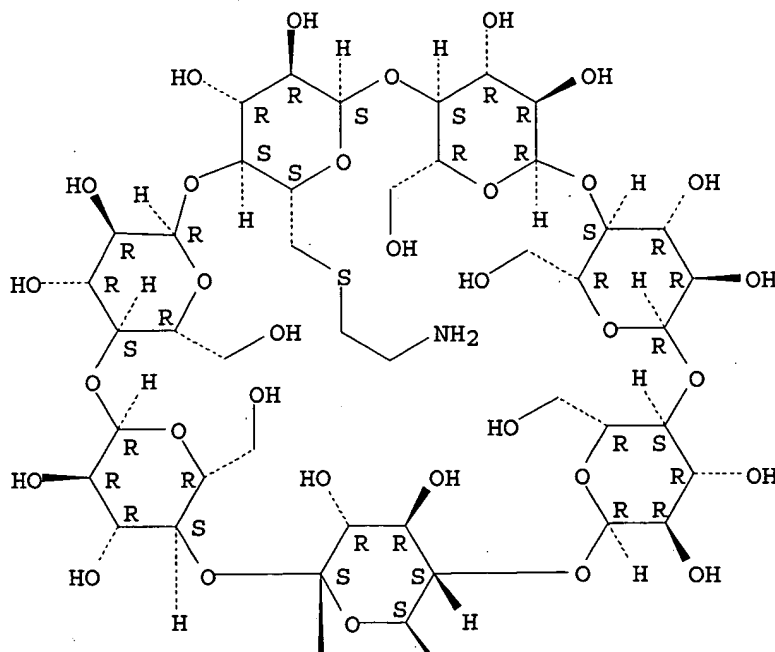
CM 3

CRN 101652-40-8

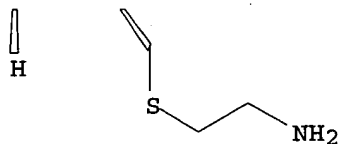
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

PAGE 1-A



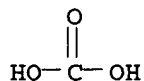
PAGE 2-A



CM 4

CRN 463-79-6

CMF C H2 O3



L55 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:400197 HCAPLUS

DOCUMENT NUMBER: 135:227176

TITLE: Difunctionalized β -cyclodextrins: synthesis and X-ray diffraction structure of 6I,6II-dideoxy-6I,6II-bis[2-(2-pyridyl)ethylamino]- β -cyclomaltoheptaose

AUTHOR(S): Saviano, Michele; Benedetti, Ettore; di Blasio, Benedetto; Gavuzzo, Enrico; Fierro, Olga; Pedone,

Carlo; Iacovino, Rosa; Rizzarelli, Enrico; Vecchio, Graziella
CORPORATE SOURCE: Biocrystallography Research Centre, CNR, Naples, 80134, Italy
SOURCE: Journal of the Chemical Society, Perkin Transactions 2 (2001) (6), 946-952
CODEN JCSPGI; ISSN: 1472-779X
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:227176

AB The synthesis, solution NMR investigation and solid state structural characterization of a new difunctionalized β -cyclodextrin (β -CD) are reported. 6I,6II-Dideoxy-6I,6II-bis[2-(2-pyridyl)ethylamino]- β -cyclomaltoheptaose is synthesized for the first time using a regioselective synthetic procedure. On the basis of an aqueous solution NMR investigation, the intramol. interaction of the two pyridine rings with the upper rim of the cavity is proposed. 6I,6II-Dideoxy-6I,6II-bis[2-(2-pyridyl)ethylamino]- β -cyclomaltoheptaose, C₅₆H₈₆N₄O₃₃, crystallizes in the monoclinic P2₁ space group with cell dimension $a = 26.303(5)$, $b = 15.670(5)$, $c = 8.276(2)$ Å and $\beta = 103.60(2)^\circ$, and 5.5 mols. of water for each independent β -cyclodextrin mol. The structure refines to $R = 0.103$ for 2270 observed reflections [$I \geq 3\sigma(I)$] and represents the first example of a complete structural characterization of a branched difunctionalized β -cyclodextrin. In the solid state, the macrocycle structure maintains an approx. seven-fold symmetry with only small changes occurring in the cyclic carbohydrate conformation where two consecutive primary hydroxy groups are substituted with bulky moieties. The two aminoethylpyridine groups linked to contiguous glucosidic units show different behavior, with one group extending away from the cavity of the β -CD, the other remaining in the proximity of the 'mouth' of the cavity. However, in the crystal the aminoethylpyridine group extending away from the cavity of the β -CD is deeply inserted into the cavity of the adjacent β -CD mol. translated along the c axis, giving rise to long rows of β -CD mols. stabilized by these host-guest interactions. The resulting polymeric arrangement has already been observed in crystal structures of other monosubstituted β -CDs.

CC 33-7 (Carbohydrates)

Section cross-reference(s): 22, 75

IT 2706-56-1, 2-Pyridineethanamine 96761-41-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(regioselective synthesis and X-ray diffraction structure of 6I,6II-dideoxy-6I,6II-bis[2-(2-pyridyl)ethylamino]- β -cyclomaltoheptaose)

IT 96761-41-0

RL: RCT (Reactant); RACT (Reactant or reagent)

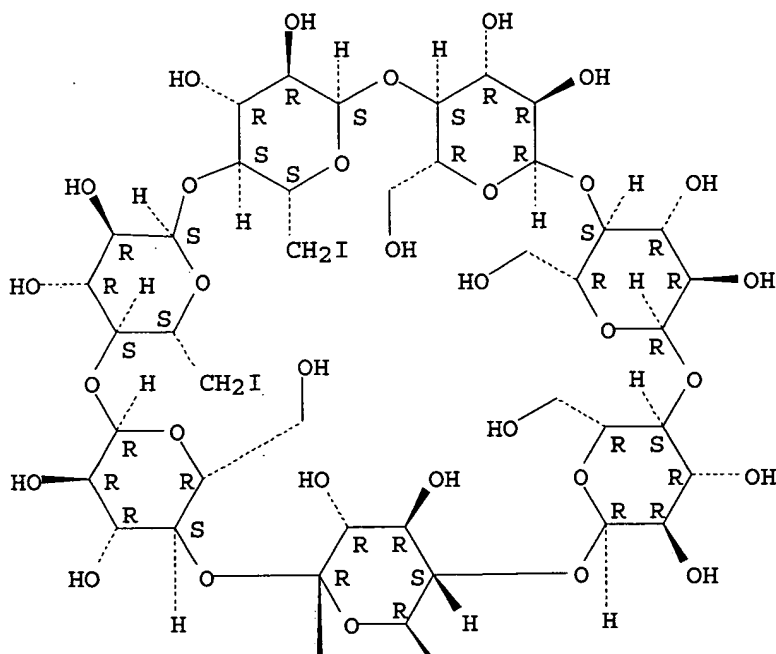
(regioselective synthesis and X-ray diffraction structure of 6I,6II-dideoxy-6I,6II-bis[2-(2-pyridyl)ethylamino]- β -cyclomaltoheptaose)

RN 96761-41-0 HCAPLUS

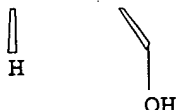
CN β -Cyclodextrin, 6A,6B-dideoxy-6A,6B-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55. ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:115591 HCAPLUS

DOCUMENT NUMBER: 134:300714

TITLE: Effects of Structure of β -Cyclodextrin-Containing Polymers on Gene Delivery

AUTHOR(S): Hwang, Suzie J.; Bellocq, Nathalie C.; Davis, Mark E

CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA

SOURCE: Bioconjugate Chemistry (2001), 12(2), 280-290

CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Linear cationic β -cyclodextrin-based polymers (BCDPs) are capable of forming polyplexes with nucleic acids and transfecting cultured cells. The BCDPs are synthesized by the condensation of a diamino-cyclodextrin monomer A with a diimide comonomer B. In this paper, the effects of polymer structure on polyplex formation,

April 5, 2004
unbr

in vitro transfection efficiency and toxicity are elucidated. By comparison of the β CDPs to polyamides lacking cyclodextrins, the inclusion of a cyclodextrin moiety in the comonomer A units reduces the IC50s of the **polymer** by up to 3 orders of magnitude. The spacing between the cationic amidine groups is also important. Different **polymers** with 4, 5, 6, 7, 8, and 10 methylene units (β CDP4, 5, 6, 7, 8, and 10) in the comonomer B mol. are synthesized. Transfection efficiency is dependent on comonomer B length with up to 20-fold difference between **polymers**. Optimum transfection is achieved with the β CDP6 **polymer**. In vitro toxicity varied by 1 order of magnitude and the lowest toxicity is observed with β CDP8. The LD40 of the β CDP6 to mice is 200 mg/kg, making this **polymer** a promising agent for in vivo gene delivery applications.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 33

ST cyclodextrin contg **polymer** structure gene delivery

IT Drug delivery systems

(gene; structure of β -cyclodextrin-containing **polymers** on gene delivery)

IT Electron density

Gene therapy

Hydrophobicity

Transformation, genetic

(structure of β -cyclodextrin-containing **polymers** on gene delivery)

IT 254912-11-3P 334706-16-0P 334706-17-1P 334706-18-2P 334706-19-3P
334706-20-6P

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(structure of β -cyclodextrin-containing **polymers** on gene delivery)

IT 60-23-1, Cysteamine 124-09-4, 1,6-Hexanediamine, reactions 1675-69-0, Azelanitrile 1871-96-1, Sebaconitrile 3406-84-6, Biphenyl-4,4'-disulfonyl chloride 4543-66-2, Dodecanedinitrile 7585-39-9, β -Cyclodextrin 14620-72-5, Dimethyladipimide dihydrochloride 34490-86-3, Dimethylsuberimide dihydrochloride 58537-94-3, Dimethylpimelimide dihydrochloride

RL: RCT (Reactant); RACT (Reactant or reagent)

(structure of β -cyclodextrin-containing **polymers** on gene delivery)

IT 60998-60-9P, Decanediimidic acid, dimethyl ester, dihydrochloride 71160-06-0P, Dodecanediimidic acid, dimethyl ester, dihydrochloride 73499-21-5P 76700-72-6P 101652-40-8P 275354-58-0P 275354-59-1P 334706-03-5P 334706-14-8P 334706-15-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(structure of β -cyclodextrin-containing **polymers** on gene delivery)

IT 76700-72-6P 101652-40-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

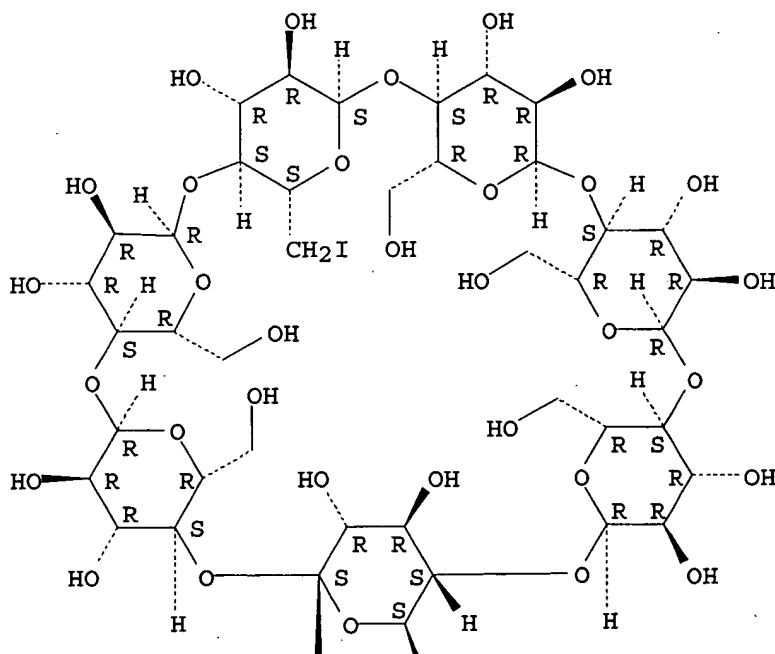
(structure of β -cyclodextrin-containing **polymers** on gene delivery)

RN 76700-72-6 HCAPLUS

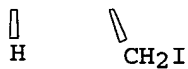
CN β -Cyclodextrin, 6A,6D-dideoxy-6A,6D-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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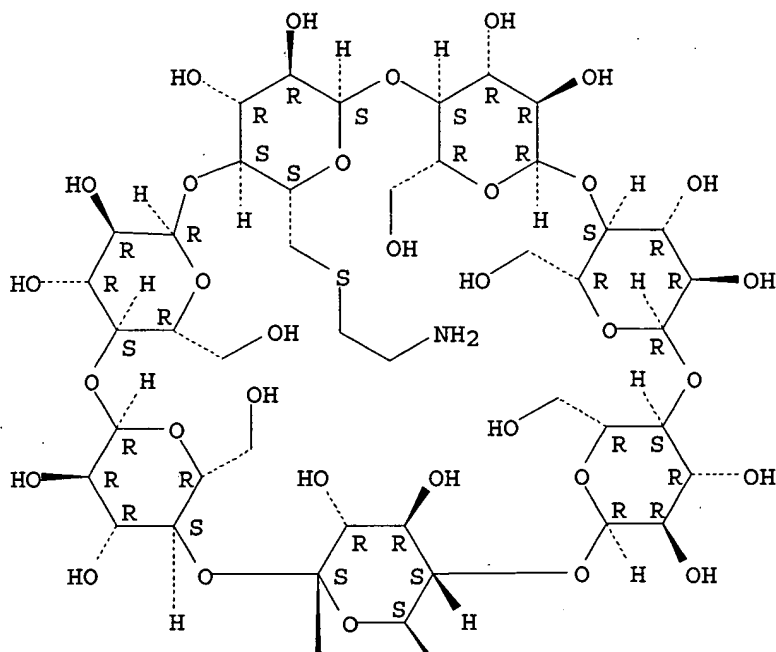


RN 101652-40-8 HCAPLUS

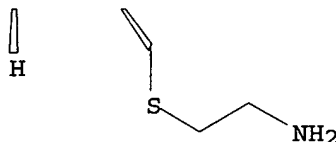
CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:23591 HCAPLUS

DOCUMENT NUMBER: 134:281423

TITLE: Chiral β -cyclodextrin-based **polymer** supports prepared via ring-opening metathesis graft-**polymerization**

AUTHOR(S): Mayr, B.; Sinner, F.; Buchmeiser, M. R.

CORPORATE SOURCE: Institute of Analytical Chemistry and Radiochemistry, University of Innsbruck, Innsbruck, A-6020, Austria

SOURCE: Journal of Chromatography, A (2001), 907(1-2), 47-56
CODEN: JCRAEY; ISSN: 0021-9673

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of norborn-2-ene-derivatized β -cyclodextrins (β -CDs), 6-O-(norborn-2-ene-5-carboxyl)- β -CD (1), tetrakis(6-O-norborn-2-ene-5-carboxyl)- β -CD (2), 6-O-(7-oxanorborn-2-ene-5-carboxyl)- β -CD (3), 6-O-(6-norborn-2-ene-5-carbonylamino)hexoxyl)- β -CD (4),

6-O-(norborn-2-ene-5-ylmethoxymethylsilyl)- β -CD (5), tris(6-O-norborn-2-ene-5-ylmethoxymethylsilyl)- β -CD (6), tetrakis(6-O-norborn-2-ene-5-ylmethoxymethylsilyl)- β -CD (7) and hexakis(6-O-norborn-2-ene-5-ylmethoxymethylsilyl)- β -CD (8), was synthesized. Compds. 1-3 were prepared via reaction of β -CD with norborn-2-ene-5-carboxylic chloride and 7-oxanorborn-2-ene-5-carboxylic chloride, resp.; compds. 5-8 were synthesized from norborn-2-ene-5-yl-methyldichlorosilane and β -CD, resp. Compound 4 was accessible by reaction of norborn-2-ene-5-carboxylamino hexoyl chloride with β -CD. Compds. 1-8 were surface grafted onto norborn-2-ene-derivatized silica-based supports using ring-opening metathesis **polymn.** employing the ruthenium-based initiator bis(tricyclohexylphosphino)benzylideneruthenium dichloride [$\text{Cl}_2\text{Ru}(\text{CHC}_6\text{H}_5)(\text{PCy}_3)_2$, Cy=cyclohexyl]. Generally speaking, the resulting chiral stationary phases (CSPs) I-VIII may be prepared with high reproducibility and may be used within a pH of 2-10. Thus, relative standard deviations (σ_n -1) of the mean resolution (R_s) are <7%. The CSPs were used for the enantioselective separation of β -blockers, N-dansyl-, N-3,5-dinitrobenzoyl- and Fmoc-protected amino acids and were characterized in terms of chemical stability, selectivity (α') and resolution (R_s). Addnl., the role of the spacer as well as influences of capacity and the degree of substitution of the β -CD moiety on the separation characteristics were determined

- CC 37-3 (Plastics Manufacture and Processing)
Section cross-reference(s): 34, 38, 44, 80
- ST chiral cyclodextrin **polymer** metathesis graft **polymn.**;
amino acid enantioselective sepn silica support; norbornene deriv
cyclodextrin **polymer** graft silica; ruthenium catalyst metathesis
polymn norbornene cyclodextrin
- IT Liquid chromatographic stationary phases
(chiral cyclodextrin-based **polymer** supports prepared via
ring-opening metathesis graft-**polymn.** for enantioselectic
separation of amino acids)
- IT Amino acids, preparation
RL: PUR (Purification or recovery); PREP (Preparation)
(chiral cyclodextrin-based **polymer** supports prepared via
ring-opening metathesis graft-**polymn.** for enantioselectic
separation of amino acids)
- IT Polyalkenamers
RL: SPN (Synthetic preparation); TEM (Technical or engineered material
use); PREP (Preparation); USES (Uses)
(chiral cyclodextrin-based **polymer** supports prepared via
ring-opening metathesis graft-**polymn.** for enantioselectic
separation of amino acids)
- IT **Polymerization** catalysts
(metathetic, ring-opening, ruthenium compound; chiral cyclodextrin-based
polymer supports prepared via ring-opening metathesis graft-
polymn. for enantioselectic separation of amino acids)
- IT **Polymerization**
(metathetic, ring-opening; chiral cyclodextrin-based **polymer**
supports prepared via ring-opening metathesis graft-**polymn.** for
enantioselectic separation of amino acids)
- IT 172222-30-9
RL: CAT (Catalyst use); USES (Uses)
(catalysts; chiral cyclodextrin-based **polymer** supports prepared
via ring-opening metathesis graft-**polymn.** for enantioselectic
separation of amino acids)
- IT 525-66-6P, Propranolol 1098-50-6P, DNS-valine 1104-36-5P,
DNS-phenylalanine 6620-60-6P, Proglumide 17039-58-6P, DNS-methionine
19461-29-1P, DNS-tryptophan 29122-68-7P, Atenolol 35021-12-6P,

DNS-serine 35021-16-0P 35661-40-6P 51384-51-1P, Metoprolol
77495-25-1P 83037-88-1P 97878-75-6P

RL: PUR (Purification or recovery); PREP (Preparation)
(chiral cyclodextrin-based **polymer** supports prepared via
ring-opening metathesis graft-**polymn.** for enantioselectic
separation of)

IT 332363-47-0DP, graft **polymers** with norbornene-derivatized
silica-based supports

RL: SPN (Synthetic preparation); TEM (Technical or engineered material
use); PREP (Preparation); USES (Uses)

(monomers; preparation and application for enantioselectic separation of
amino acids)

IT 330218-57-0P 332363-47-0P 332363-48-1P 332363-49-2P 332363-50-5P
332363-51-6P 332363-52-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

(monomers; preparation and metathesis graft **polymn.** with
norbornene-derivatized silica-based supports)

IT 332363-46-9P

RL: SPN (Synthetic preparation); TEM (Technical or engineered material
use); PREP (Preparation); USES (Uses)

(monomers; preparation and metathesis graft **polymn.** with
norbornene-derivatized silica-based supports)

IT 14319-64-3DP, reaction products with silica support, graft
polymers with norbornene-containing cyclodextrin 119792-17-5DP,
Nucleosil 300-5, reaction products with trichloronorbornenesilane, graft
polymers with norbornene-containing cyclodextrin 330218-57-0DP,
graft **polymers** with norbornene-derivatized silica-based supports
332363-46-9DP, graft **polymers** with norbornene-derivatized
silica-based supports 332363-48-1DP, graft **polymers** with
norbornene-derivatized silica-based supports 332363-49-2DP, graft
polymers with norbornene-derivatized silica-based supports
332363-50-5DP, graft **polymers** with norbornene-derivatized
silica-based supports 332363-51-6DP, graft **polymers** with
norbornene-derivatized silica-based supports 332363-52-7DP, graft
polymers with norbornene-derivatized silica-based supports
RL: SPN (Synthetic preparation); TEM (Technical or engineered material
use); PREP (Preparation); USES (Uses)
(preparation and application for enantioselectic separation of amino acids)

IT 332363-51-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

(monomers; preparation and metathesis graft **polymn.** with
norbornene-derivatized silica-based supports)

RN 332363-51-6 HCAPLUS

CN β -Cyclodextrin, 6A,6B,6?,6?-tetrakis-O-(bicyclo[2.2.1]hept-5-en-2-
ylmethoxymethylsilyl)- (9CI) (CA INDEX NAME)

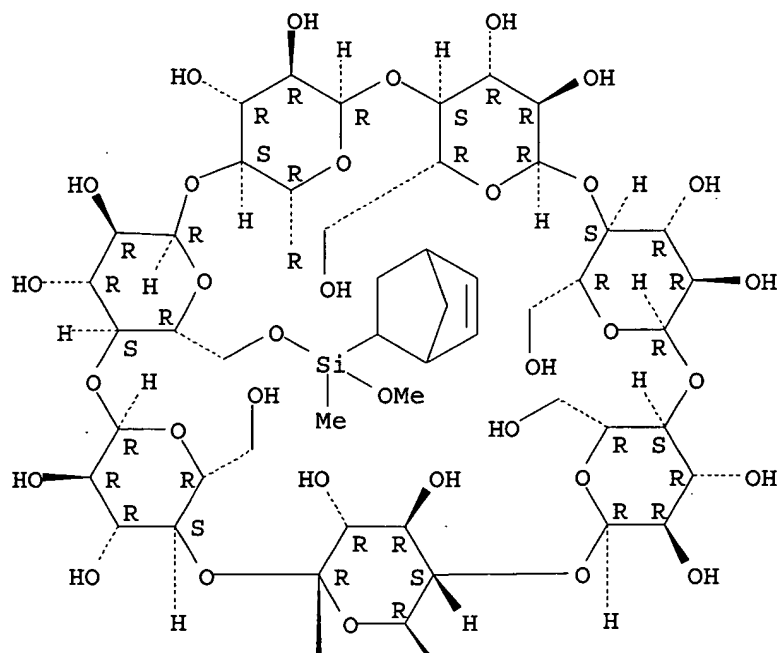
CM 1

CRN 336128-22-4

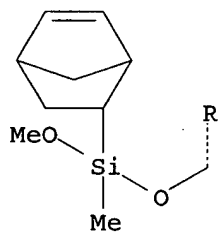
CMF C60 H98 O37 Si2

Absolute stereochemistry.

PAGE 1-A

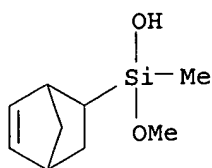


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CM 2

CRN 302598-12-5
 CMF C9 H16 O2 Si



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2000:401687 HCAPLUS
 DOCUMENT NUMBER: 133:48948
 TITLE: Supramolecular complexes containing therapeutic agents
 INVENTOR(S): Davis, Mark E.; Gonzalez, Hector; Hwang, Suzie
 PATENT ASSIGNEE(S): California Institute of Technology, USA
 SOURCE: PCT Int. Appl., 70 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000033885	A1	20000615	WO 1999-US28547	19991203
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1133318	A1	20010919	EP 1999-965967	19991203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002531530	T2	20020924	JP 2000-586375	19991203
PRIORITY APPLN. INFO.: US 1998-110847P P 19981204 US 1999-127856P P 19990405 WO 1999-US28547 W 19991203				
AB A method of preparing a supramol. complex containing at least one therapeutic agent and a multi-dimensional polymer network is described. A supramol. complex prepared by a method of the invention is described. A method of treatment by administering a therapeutically effective amount of a supramol. complex of the invention is also described. Such a supramol. complex may be used as a delivery vehicle for various therapeutic agents. The polymers include linear or branched polyethyleneimine and cyclodextrin derivs.				
IC ICM A61K047-48 ICS A61K031-335; A61K031-70				
CC 63-6 (Pharmaceuticals)				
ST drug polymer network complex prepn; cyclodextrin drug ligand complex delivery vehicle				
IT 9002-98-6DP, Polyethylenimine, reaction product with β -cyclodextrinethiol and functionalized PEG 25322-68-3DP, PEG, reaction product with β -cyclodextrinethiol and polyethylenimine 29390-66-7P				

35625-91-3P 39927-08-7P 52539-19-2P 67217-55-4P 73499-21-5P
 76700-72-6P 81644-55-5DP, reaction product with functionalized
 PEG and polyethylenimine 81644-55-5P 98126-99-9P
 101652-40-8P 254912-03-3P 254912-04-4P
 254912-05-5DP, oxidized 254912-05-5P
 254912-07-7P 254912-09-9P 275354-50-2P
 275354-52-4DP, reaction products with DNA 275354-53-5P
 275354-54-6P 275354-55-7P 275354-57-9P
 275354-58-0P 275354-59-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)

(preparation of supramol. complexes containing therapeutic agents)

IT 76700-72-6P 98126-99-9P 101652-40-8P
 254912-03-3P 254912-04-4P 254912-05-5DP,
 oxidized 254912-05-5P 254912-07-7P
 254912-09-9P 275354-52-4DP, reaction products with DNA
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)

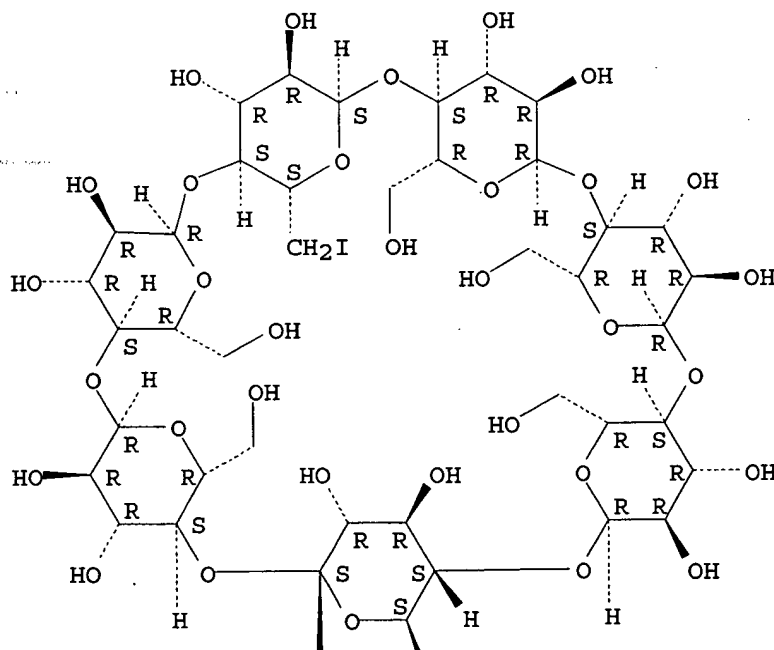
(preparation of supramol. complexes containing therapeutic agents)

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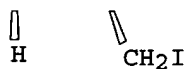
CN β -Cyclodextrin, 6A,6D-dideoxy-6A,6D-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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PAGE 2-A

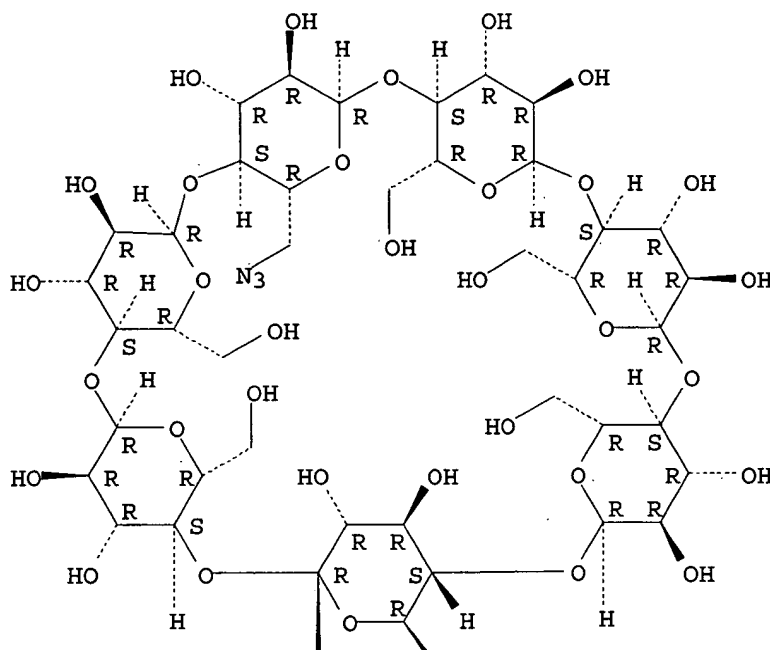


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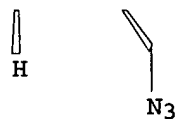
CN β -Cyclodextrin, 6A,6D-diazido-6A,6D-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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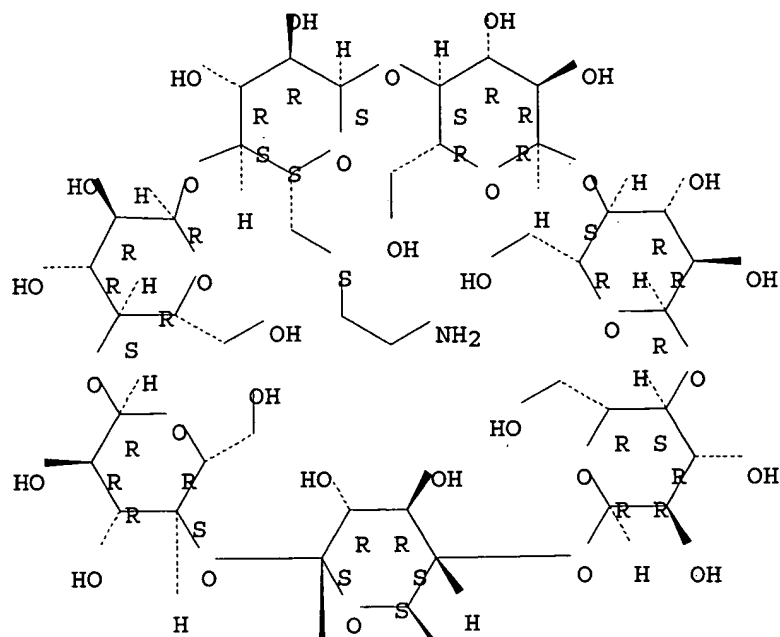


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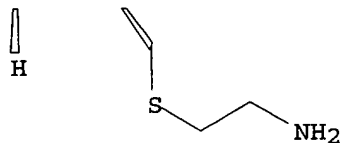
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Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



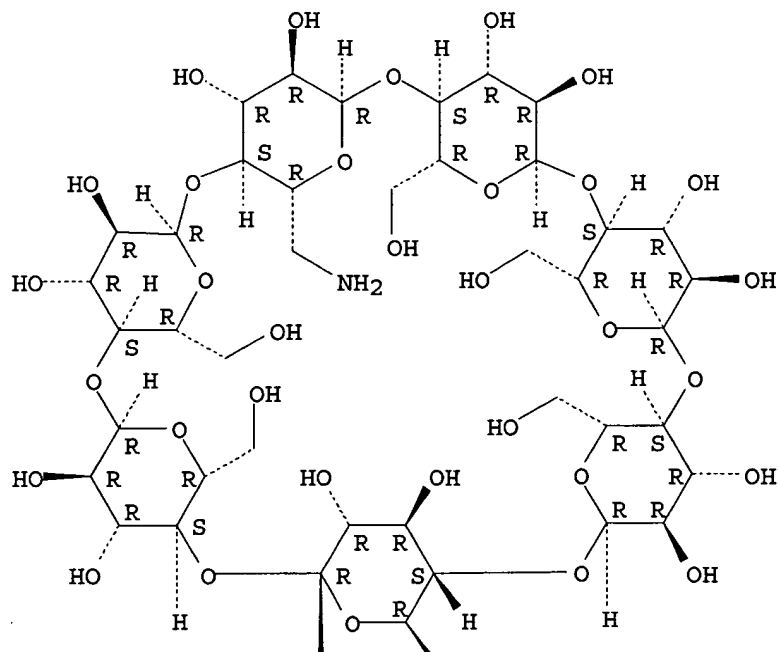
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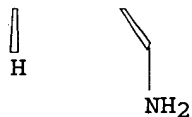
CRN 162825-08-3
 CMF C42 H72 N2 O33

Absolute stereochemistry.

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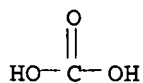
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CM 2

CRN 463-79-6

CMF C H2 O3



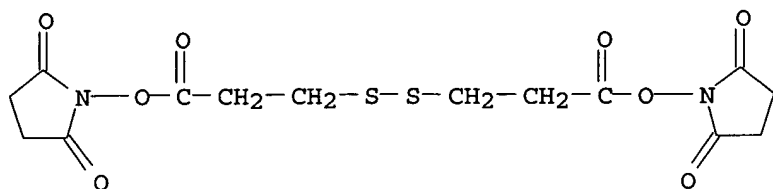
RN 254912-04-4 HCAPLUS

CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2),
polymer with 1,1'-[dithiobis[(1-oxo-3,1-propanediyl)oxy]]bis[2,5-
pyrrolidinedione] (9CI) (CA INDEX NAME)

CM 1

CRN 57757-57-0

CMF C14 H16 N2 O8 S2



CM 2

CRN 254912-03-3

CMF C42 H72 N2 O33 . 2 C H2 O3

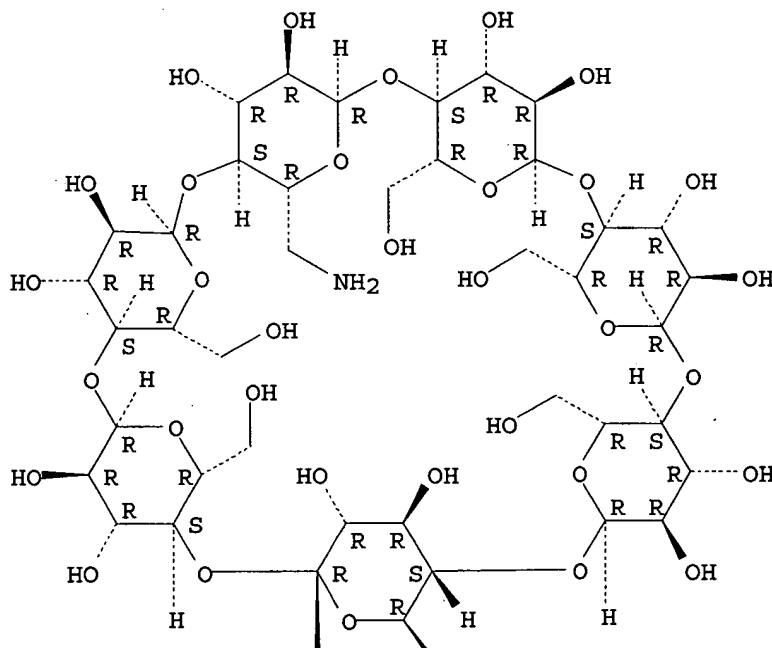
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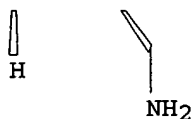
CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



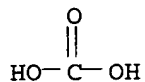
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CM 4

CRN 463-79-6

CMF C H2 O3



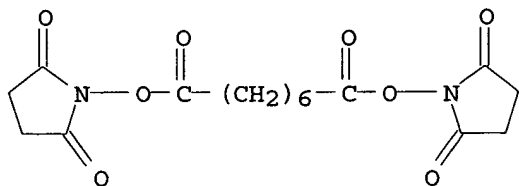
RN 254912-05-5 HCAPLUS

CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2),
polymer with 1,1'-[(1,8-dioxo-1,8-octanediyl)bis(oxy)]bis[2,5-
pyrrolidinedione] (9CI) (CA INDEX NAME)

CM 1

CRN 68528-80-3

CMF C16 H20 N2 O8



CM 2

CRN 254912-03-3

CMF C42 H72 N2 O33 . 2 C H2 O3

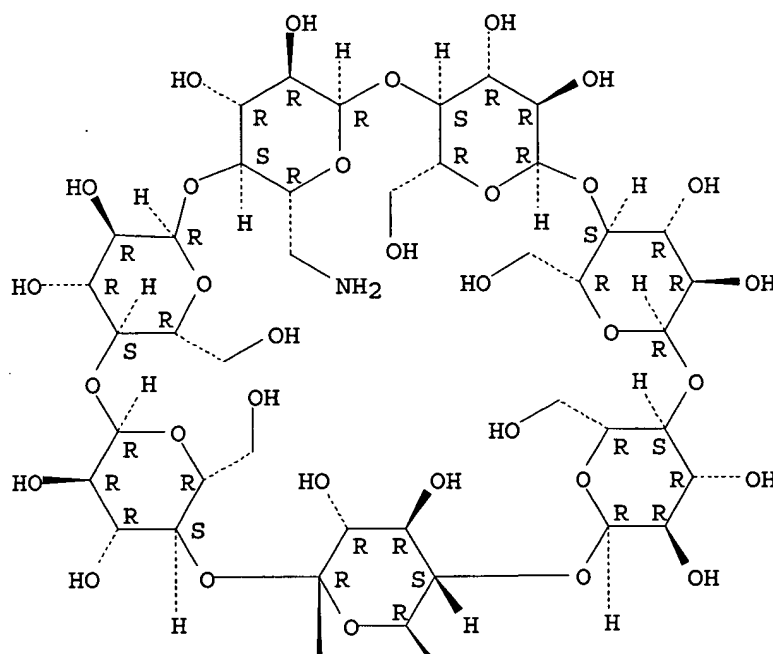
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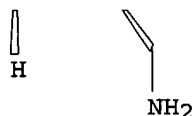
CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



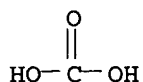
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CM 4

CRN 463-79-6

CMF C H2 O3



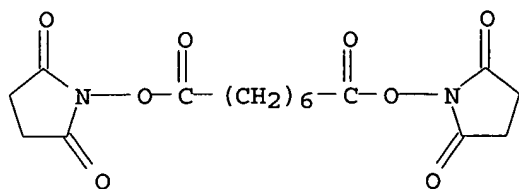
RN 254912-05-5 HCAPLUS

CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2),
polymer with 1,1'-[(1,8-dioxo-1,8-octanediyl)bis(oxy)]bis[2,5-
pyrrolidinedione] (9CI) (CA INDEX NAME)

CM 1

CRN 68528-80-3

CMF C16 H20 N2 O8



CM 2

CRN 254912-03-3

CMF C42 H72 N2 O33 . 2 C H2 O3

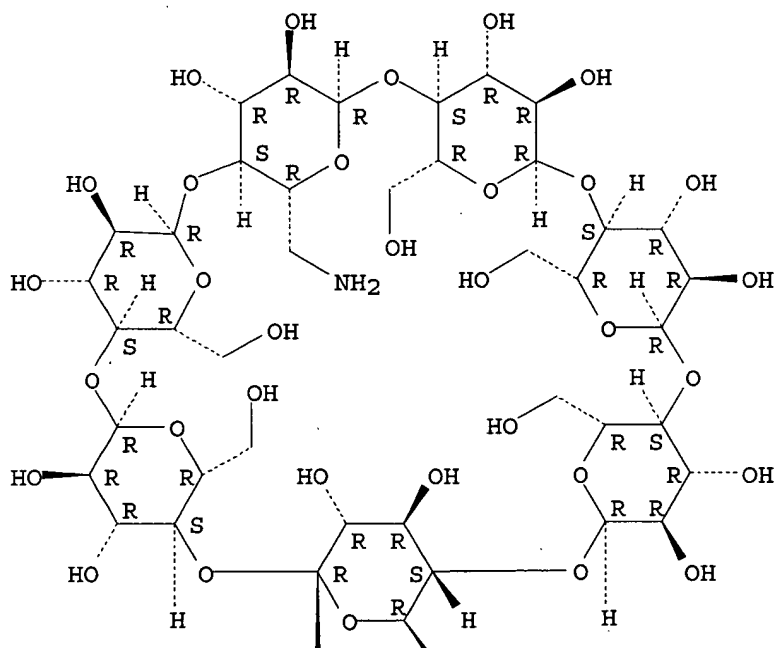
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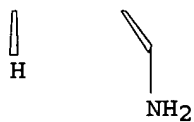
CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



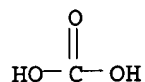
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CM 4

CRN 463-79-6

CMF C H2 O3



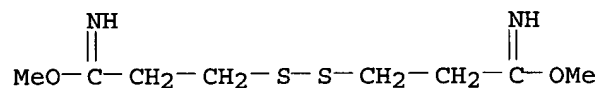
RN 254912-07-7 HCAPLUS

CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2),
polymer with dimethyl 3,3'-dithiobis[propanimidate] dihydrochloride (9CI)
(CA INDEX NAME)

CM 1

CRN 38285-78-8

CMF C8 H16 N2 O2 S2 . 2 Cl H



●2 HCl

CM 2

CRN 254912-03-3

CMF C42 H72 N2 O33 . 2 C H2 O3

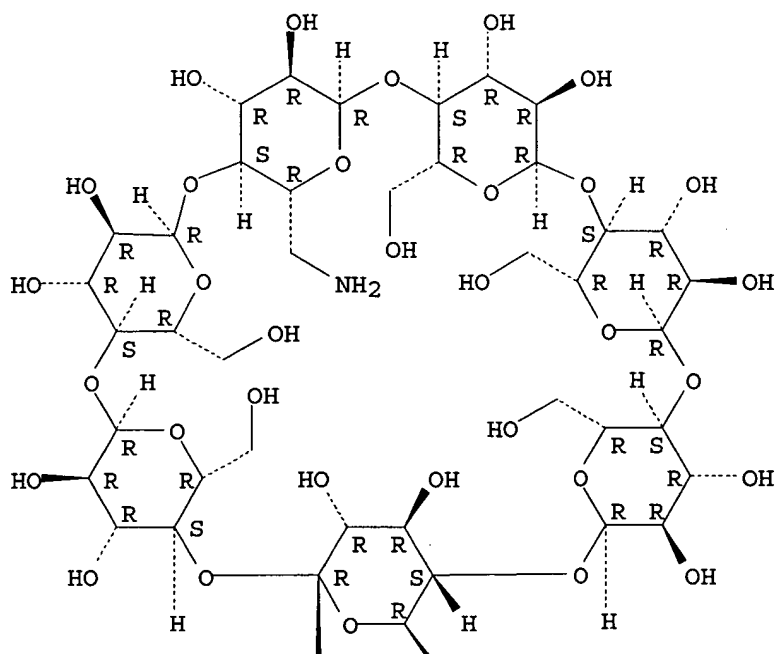
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CRN 162825-08-3

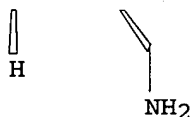
CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



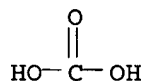
PAGE 2-A



CM 4

CRN 463-79-6

CMF C H2 O3



RN 254912-09-9 HCAPLUS

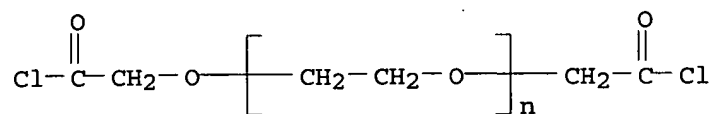
CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2),
polymer with α -(2-chloro-2-oxoethyl)- ω -(2-chloro-2-oxoethoxy)poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

CM 1

CRN 35625-91-3

CMF (C2 H4 O)_n C4 H4 Cl2 O3

CCI PMS



CM 2

CRN 254912-03-3

CMF C42 H72 N2 O33 . 2 C H2 O3

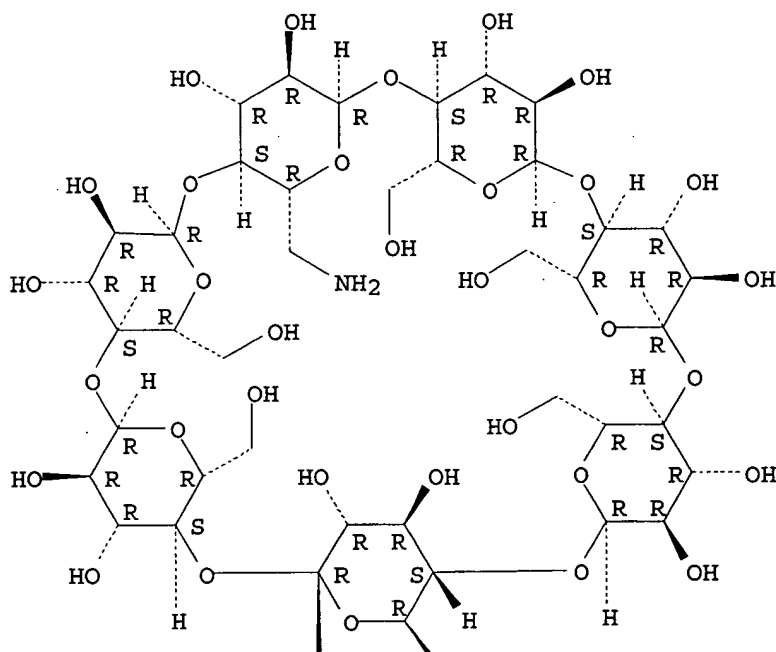
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CRN 162825-08-3

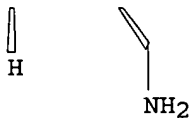
CMF C42 H72 N2 O33

Absolute stereochemistry.

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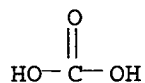
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CM 4

CRN 463-79-6

CMF C H2 O3



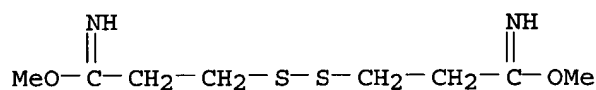
RN 275354-52-4 HCAPLUS

CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, carbonate
(1:2) (salt), polymer with dimethyl 3,3'-dithiobis[propanimidate]
dihydrochloride (9CI) (CA INDEX NAME)

CM 1

CRN 38285-78-8

CMF C8 H16 N2 O2 S2 . 2 Cl H



● 2 HCl

CM 2

CRN 275354-51-3

CMF C46 H80 N2 O33 S2 . 2 C H2 O3

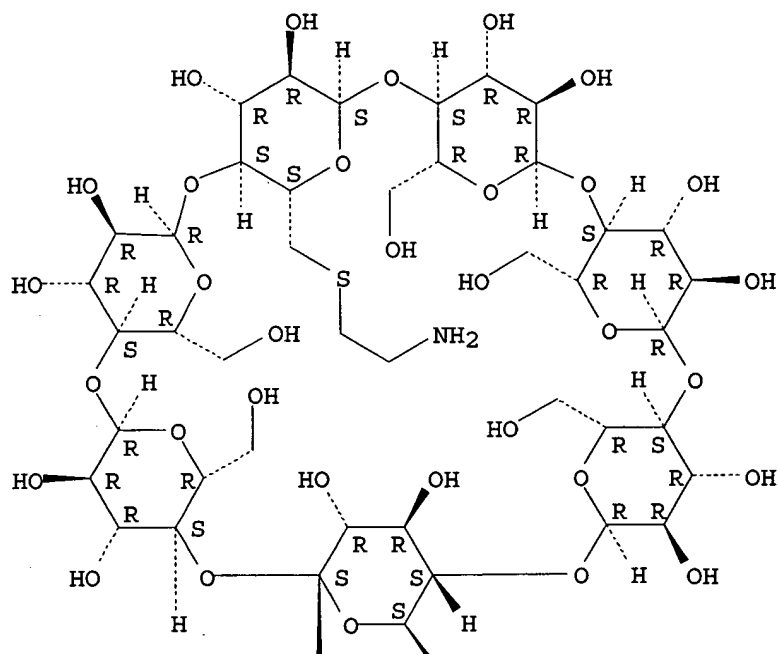
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CRN 101652-40-8

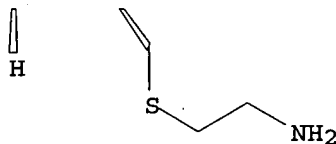
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

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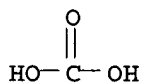
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CM 4

CRN 463-79-6

CMF C H2 O3



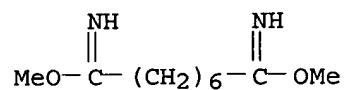
RN 275354-53-5 HCAPLUS

CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, carbonate
(1:2) (salt), polymer with dimethyl octanediimide dihydrochloride (9CI)
(CA INDEX NAME)

CM 1

CRN 34490-86-3

CMF C10 H20 N2 O2 . 2 Cl H



● 2 HCl

CM 2

CRN 275354-51-3

CMF C46 H80 N2 O33 S2 . 2 C H2 O3

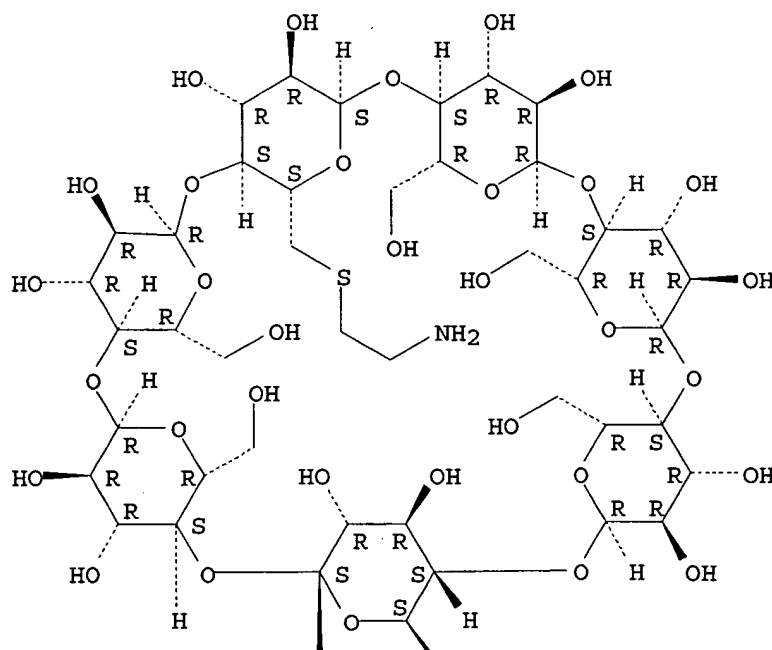
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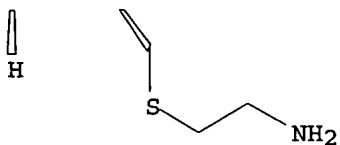
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

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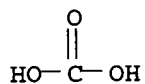
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CM 4

CRN 463-79-6

CMF C H2 O3



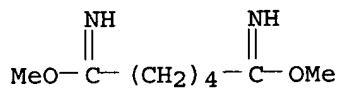
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CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, carbonate
(1:2) (salt), polymer with dimethyl hexanediimide dihydrochloride (9CI)
(CA INDEX NAME)

CM 1

CRN 14620-72-5

CMF C8 H16 N2 O2 . 2 Cl H



●2 HCl

CM 2

CRN 275354-51-3

CMF C46 H80 N2 O33 S2 . 2 C H2 O3

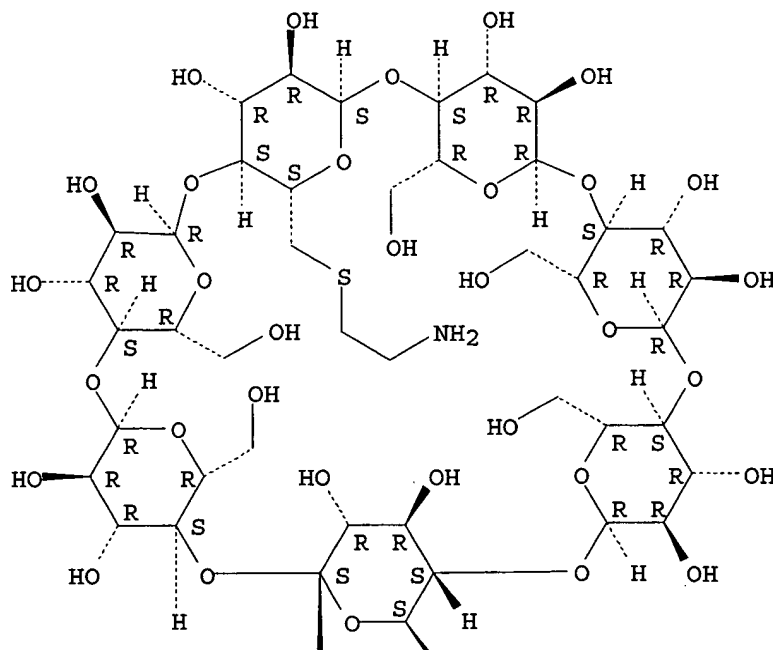
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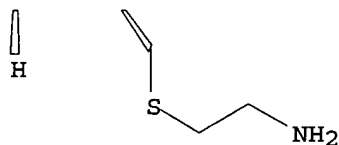
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

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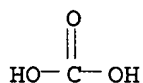
PAGE 2-A



CM 4

CRN 463-79-6

CMF C H2 O3



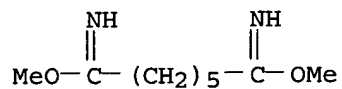
RN 275354-55-7 HCAPLUS

CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, carbonate
(1:2) (salt), polymer with dimethyl heptanediimide dihydrochloride (9CI)
(CA INDEX NAME)

CM 1

CRN 58537-94-3

CMF C9 H18 N2 O2 . 2 Cl H



● 2 HCl

CM 2

CRN 275354-51-3

CMF C46 H80 N2 O33 S2 . 2 C H2 O3

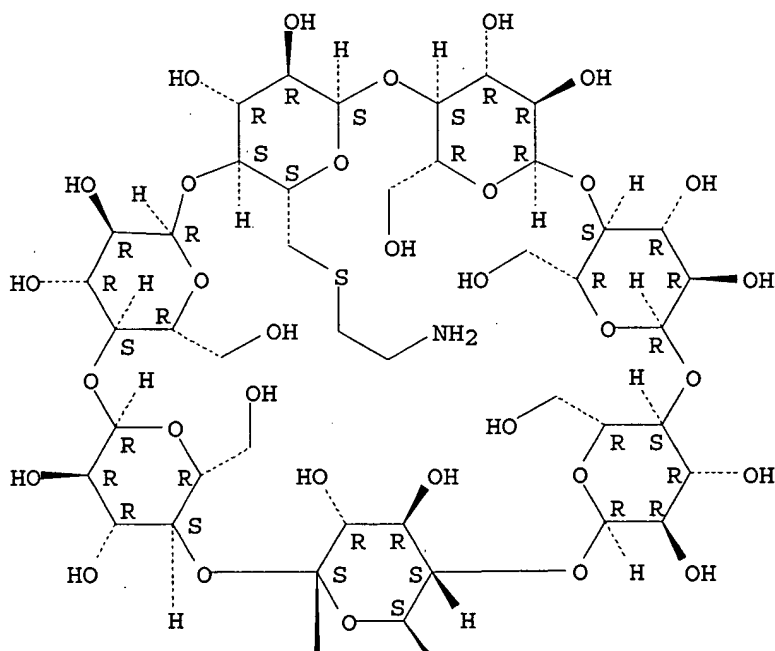
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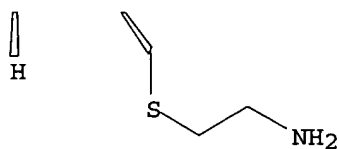
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

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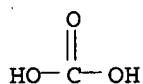
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CM 4

CRN 463-79-6

CMF C H2 O3



RN 275354-57-9 HCAPLUS

CN β-Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, polymer with α-(chloroacetyl)-ω-[(chloroacetyl)oxy]poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

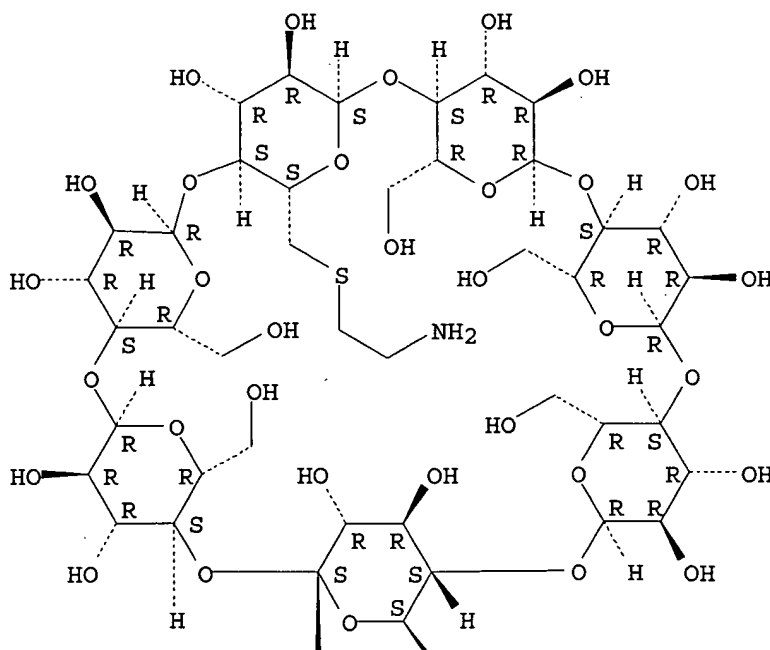
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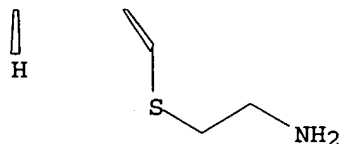
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

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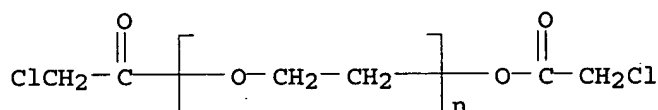


CM 2

CRN 56867-89-1

CMF (C2 H4 O)_n C4 H4 Cl2 O3

CCI PMS



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2000:34909 HCAPLUS
 DOCUMENT NUMBER: 132:94914
 TITLE: Preparation of linear cyclodextrin **copolymers**
 INVENTOR(S): Gonzalez, Hector; Hwang, Suzie Sue Jean; Davis, Mark E.
 PATENT ASSIGNEE(S): California Institute of Technology, USA
 SOURCE: PCT Int. Appl., 84 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

Appl's own work

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000001734	A1	20000113	WO 1999-US14298	19990625
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6509323	B1	20030121	US 1998-203556	19981202
CA 2336390	AA	20000113	CA 1999-2336390	19990625
AU 9948305	A1	20000124	AU 1999-48305	19990625
AU 763114	B2	20030710		
EP 1093469	A1	20010425	EP 1999-931889	19990625

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

BR 9911754	A	20011106	BR 1999-11754	19990625
JP 2002519482	T2	20020702	JP 2000-558134	19990625
US 2002151523	A1	20021017	US 2002-97326	20020315

PRIORITY APPLN. INFO.:

US 1998-91550P	P	19980701
US 1998-203556	A	19981202
US 1999-339818	A3	19990625
WO 1999-US14298	W	19990625

- AB Linear cyclodextrin **copolymers** containing an unoxidized and/or an oxidized cyclodextrin moiety integrated into the **polymer** backbone, useful as drug delivery vehicles, were prepared. For example, substitution reaction of 6A,6D-diiodo-6A,6D-deoxy- β -cyclodextrin (2-step preparation by a known procedure given) with NaSCH₂CH₂NH₂ gave 79% 6A,6D-bis(2-aminoethylthio)-6A6D-deoxy- β -cyclodextrin. This was stirred for 18 h at 80° in DMF under N with an equiv of MeOC(:NH)(CH₂)₆C(:NH)OMe-2HCl in the presence of Et₃N to give 18% of a title **copolymer** (CD **copolymer**). Media containing doxorubicin and CD **copolymer**-doxorubicin complex (general complexation procedure given) were applied to cultured cell lines to show no toxicity to KB or KB-VI cell lines in the absence of doxorubicin.
- IC ICM C08B037-16
ICS C08G081-00; C08G069-00; C08G069-40; C08G073-02; C08G073-06;
C08G075-00; A61K047-40
- CC 44-6 (Industrial Carbohydrates)
Section cross-reference(s): 63
- ST cyclodextrin linear **copolymer** prepn drug delivery;
iododeoxycyclodextrin prepn substitution aminoethylthiocyclodextrin;
aminoethylthiocyclodextrin prepn **polymn** dimethylsuberimide;
doxorubicin complex aminoethylthiocyclodextrin dimethylsuberimide
copolymer cell toxicity
- IT Drug delivery systems
(preparation of linear cyclodextrin **copolymers** as)
- IT 51178-68-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(acid chlorination; preparation of linear cyclodextrin **copolymers**
as drug delivery agents)
- IT 91190-86-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and conversion to diodo derivative; preparation of linear
cyclodextrin
copolymers as drug delivery agents)
- IT 35625-91-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and **copolymn**. with diaminocyclodextrin; preparation of
linear cyclodextrin **copolymers** as drug delivery agents)
- IT 101652-40-8P 254912-03-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation and **copolymn**.; preparation of linear cyclodextrin
copolymers as drug delivery agents)
- IT 98126-99-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation and redn to diamine; preparation of linear cyclodextrin
copolymers as drug delivery agents)
- IT 76700-72-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and substitution with sodium azide; preparation of linear cyclodextrin copolymers as drug delivery agents)

IT 23214-92-8DP, Doxorubicin, complexes with cyclodextrin copolymers
RL: BSU (Biological study, unclassified); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
(preparation of linear cyclodextrin copolymers as drug delivery agents)

IT 254912-04-4P 254912-05-5DP, oxidized 254912-05-5P 254912-07-7P
254912-08-8P 254912-09-9P 254912-10-2P 254912-11-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of linear cyclodextrin copolymers as drug delivery agents)

IT 7585-39-9, β -Cyclodextrin
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with biphenyldisulfonyl dichloride; preparation of linear cyclodextrin copolymers as drug delivery agents)

IT 3406-84-6, Biphenyl-4,4'-disulfonyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with β -cyclodextrin; preparation of linear cyclodextrin copolymers as drug delivery agents)

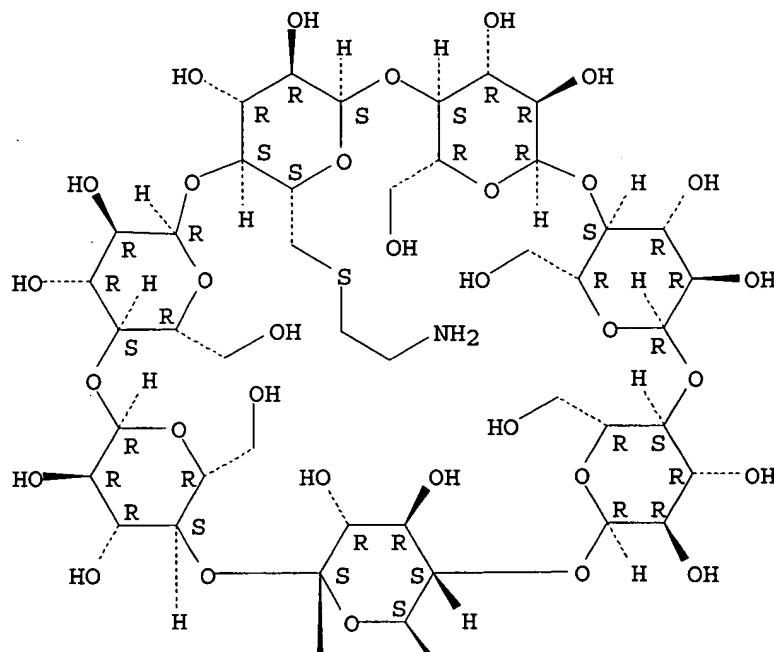
IT 51974-68-6, Sodium 2-aminoethylthiolate
RL: RCT (Reactant); RACT (Reactant or reagent)
(thioetherification of diiodocyclodextrin; preparation of linear cyclodextrin copolymers as drug delivery agents)

IT 101652-40-8P 254912-03-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and copolymn.; preparation of linear cyclodextrin copolymers as drug delivery agents)

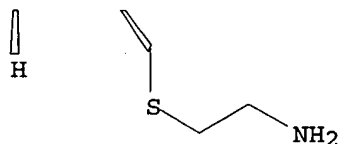
RN 101652-40-8 HCAPLUS
CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



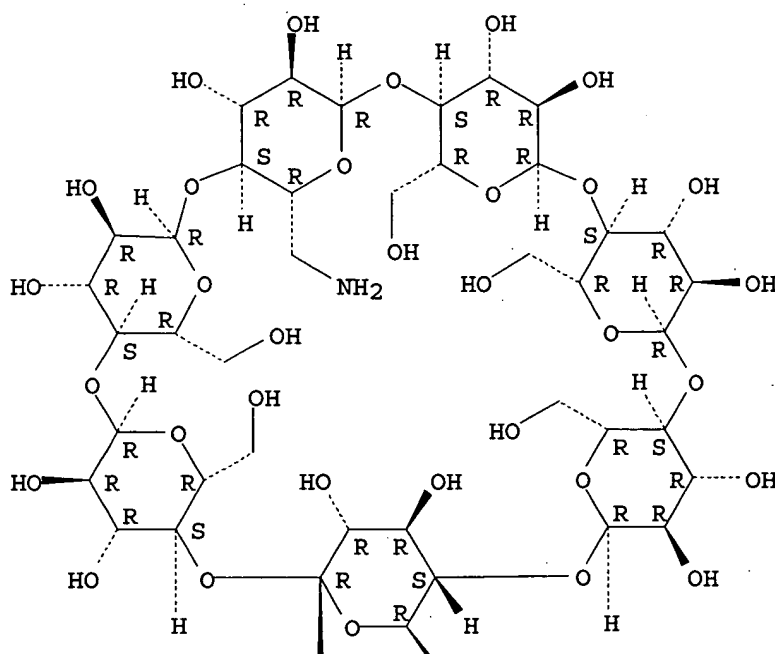
RN 254912-03-3 HCAPLUS
 CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2) (9CI)
 (CA INDEX NAME)

CM 1

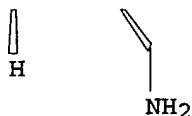
CRN 162825-08-3
 CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A

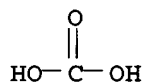


PAGE 2-A



CM 2

CRN 463-79-6
CMF C H2 O3



IT 98126-99-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

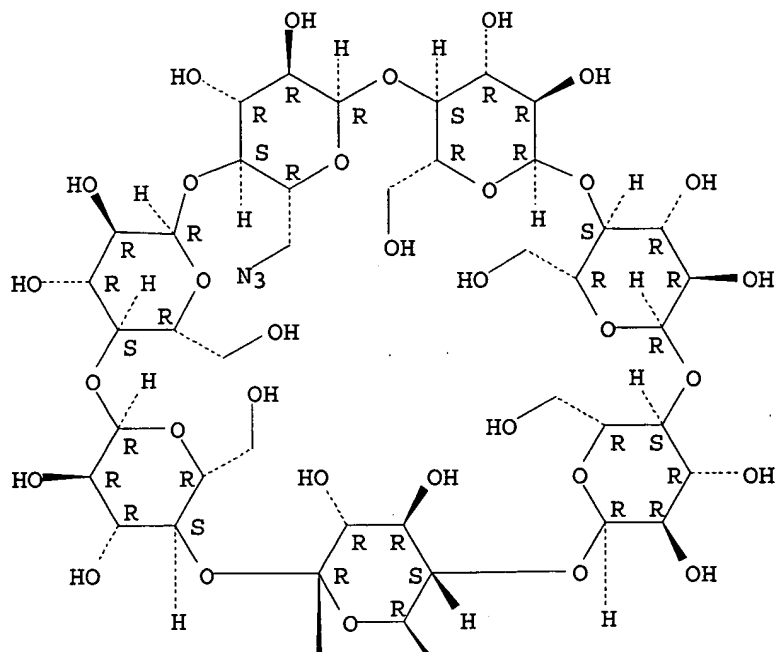
(preparation and redn to diamine; preparation of linear cyclodextrin
copolymers as drug delivery agents)

RN 98126-99-9 HCAPLUS

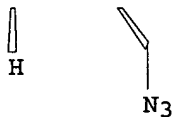
CN β -Cyclodextrin, 6A,6D-diazido-6A,6D-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT 76700-72-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

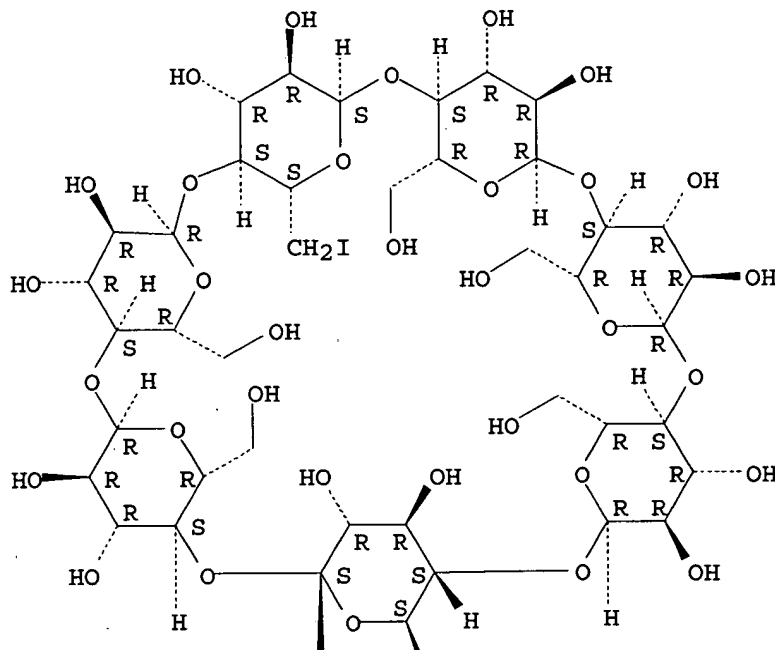
(preparation and substitution with sodium azide; preparation of linear cyclodextrin copolymers as drug delivery agents)

RN 76700-72-6 HCAPLUS

CN β -Cyclodextrin, 6A,6D-dideoxy-6A,6D-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:607456 HCAPLUS

DOCUMENT NUMBER: 132:26733

TITLE: New Class of **Polymers** for the Delivery of Macromolecular Therapeutics

AUTHOR(S): Gonzalez, Hector; Hwang, Sue Jean; Davis, M. E.
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA

SOURCE: Bioconjugate Chemistry (1999) 10(6), 1068-1074
CODEN: BCCHES; ISSN: 1044-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cationic **polymers** show promise for the in vitro and in vivo delivery of macromol. therapeutics. Known cationic **polymers**, e.g., poly(L)lysine (PLL) and polyethylenimine (PEI), have been employed in native and modified forms for the delivery of plasmid DNA (pDNA) and reveal varying levels of toxicity. Here, we report the preparation of a new class of cationic **polymers** that are specifically designed to

deliver macromol. therapeutics. Linear, cationic, β -cyclodextrin (β -CD)-containing **polymers** (CD-**polymers**) are synthesized by **copoly**mg. difunctionalized β -CD monomers (AA) with other difunctionalized comonomers (BB) such that an AABBAABB product is formed. The β -CD **polymers** are able to bind .apprx.5 kbp pDNA above **polymer** to DNA (\pm) charge ratios of 1.5, compact the bound pDNA into particles of approx. 100-150 nm in size at charge ratios above ± 5 , and transfect cultured cells at charge ratios above ± 10 . In vitro transfections with the new β -CD-**polymers** are comparable to the best results obtained in our hands with PEI and Lipofectamine. Some cell line-dependent toxicities are observed for serum-free transfections; however, no toxicity is revealed at charge ratios as high as ± 70 - in transfections conducted in 10% serum. Single IV and IP doses as high as 200 mg/kg in mice showed no mortalities.

CC 63-5 (Pharmaceuticals)

ST cyclodextrin cationic **polymer** macromol delivery

IT DNA

RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(binding; cyclodextrin cationic **polymers** for macromols. delivery)

IT DNA

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(complexes; cyclodextrin cationic **polymers** for macromols. delivery)

IT Drug delivery systems

Transformation, genetic

(cyclodextrin cationic **polymers** for macromols. delivery)

IT 29878-26-ODP, Dimethylsuberimide, alternating **copolymers** with

β -cyclodextrin derivs. 57757-57-ODP, alternating **copolymers** with β -cyclodextrin derivs. 101652-40-8DP, alternating

copolymers with dimethylsuberimide 162825-08-3DP, alternating **copolymers** with dimethylsuberimide and with dithiobis(succinimidyl propionate)

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(cyclodextrin cationic **polymers** for macromols. delivery)

IT 101652-40-8 162825-08-3, 6A,6D-Diamino-6A,6D-dideoxy- β -cyclodextrin

RL: RCT (Reactant); RACT (Reactant or reagent)

(cyclodextrin cationic **polymers** for macromols. delivery)

IT 101652-40-8DP, alternating **copolymers** with

dimethylsuberimide 162825-08-3DP, alternating

copolymers with dimethylsuberimide and with dithiobis(succinimidyl propionate)

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

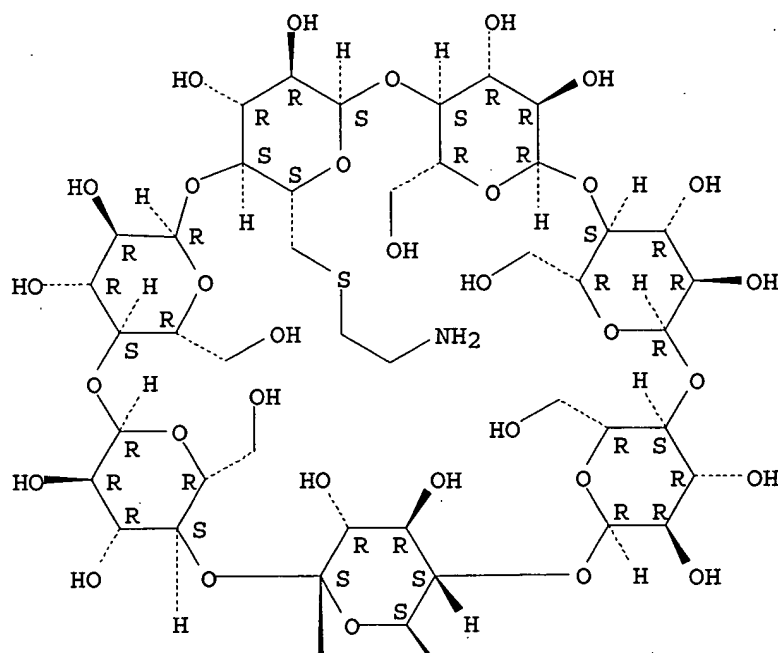
(cyclodextrin cationic **polymers** for macromols. delivery)

RN 101652-40-8 HCAPLUS

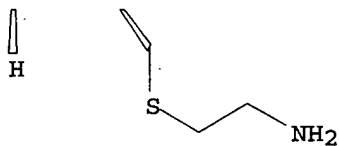
CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

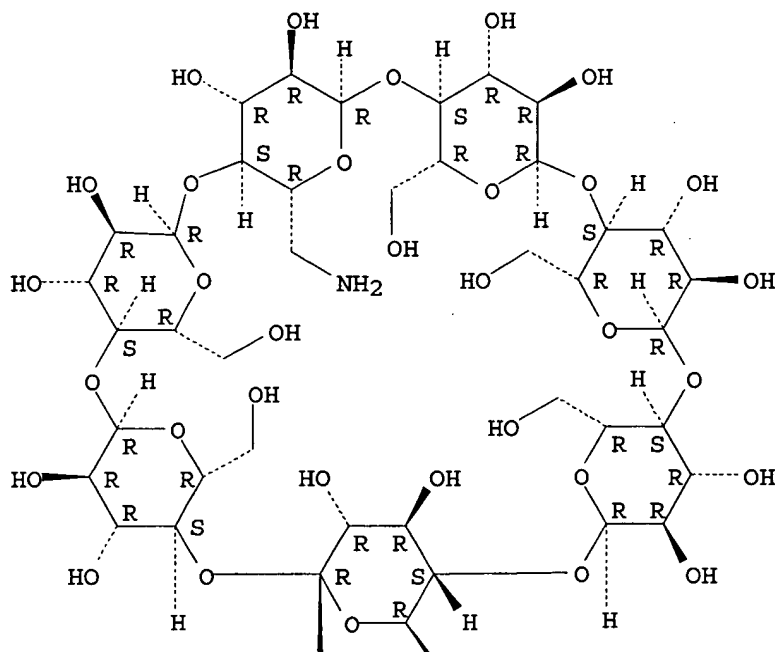


RN 162825-08-3 HCAPLUS

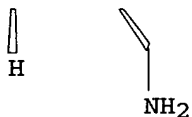
CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



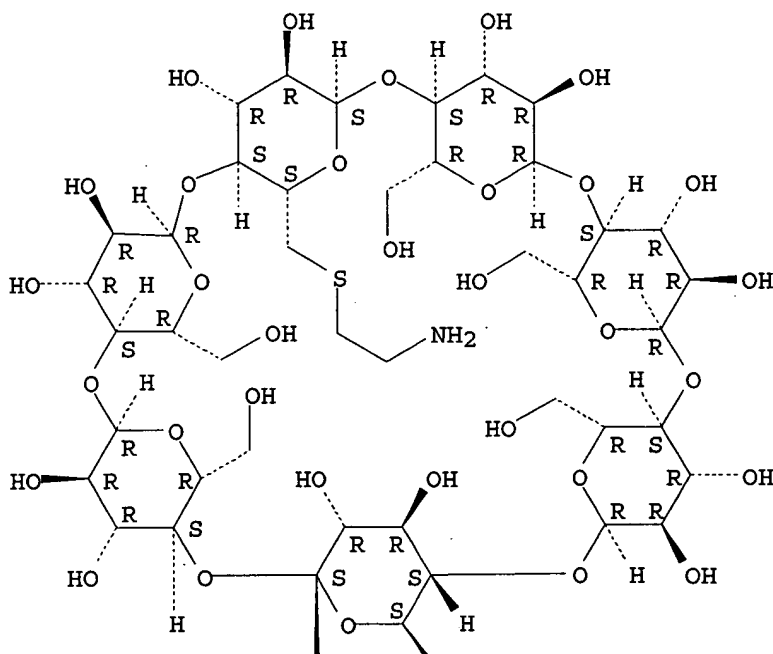
PAGE 2-A



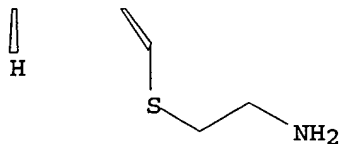
IT 101652-40-8 162825-08-3, 6A,6D-Diamino-6A,6D-dideoxy-
 β-cyclodextrin
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (cyclodextrin cationic polymers for macromols. delivery)
 RN 101652-40-8 HCAPLUS
 CN β-Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



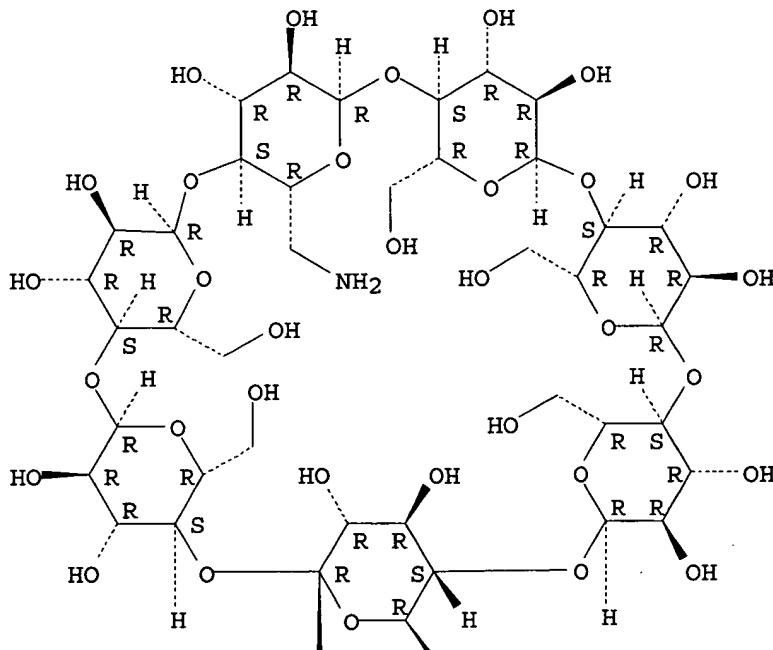
PAGE 2-A



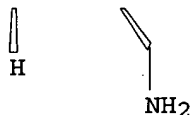
RN 162825-08-3 HCAPLUS
CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:573195 HCAPLUS

DOCUMENT NUMBER: 132:141784

TITLE: Methods to enhance the complexation efficiency of cyclodextrins

AUTHOR(S): Loftsson, T.; Masson, M.; Sigurjonsdottir, J. F.

CORPORATE SOURCE: Department of Pharmacy, University of Iceland, Reykjavik, 127, Iceland

SOURCE: S.T.P. Pharma Sciences (1999), 9(3), 237-242

CODEN: STSSE5; ISSN: 1157-1489

PUBLISHER: Editions de Sante

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In general, the complexation efficiency of cyclodextrins is rather low, and thus relatively large amts. of cyclodextrins are needed to complex small amts. of a drug. In addition, various pharmaceutical additives decrease the efficiency even further. Meanwhile, due to toxicol. considerations, formulation bulk and production cost, it is important to use as little cyclodextrin as possible in pharmaceutical preps. Several

different methods, which can be applied in order to enhance the complexation efficiency of cyclodextrins, were evaluated. A sugaring-in effect could not be observed in aqueous cyclodextrin solns. **Polymers**, and other rheol. agents, increase the complexation efficiency by increasing the apparent stability constant of the drug/cyclodextrin complex. Ionization of a drug mol. sometimes increases the complexation efficiency by increasing the intrinsic solubility of the drug. Finally, enhanced complexation efficacy can be obtained by forming a more water-soluble drug derivative of a water-insol. drug (i.e. prodrug with higher intrinsic

solubility

than the parent drug).

CC 63-5 (Pharmaceuticals)

IT 57-55-6D, 1,2-Propanediol, ether with β -cyclodextrin, reactions
7585-39-9D, β -Cyclodextrin, ethers 9000-01-5, Gum acacia
9003-39-8, Pvp 9004-54-0, Dextran, reactions 9004-65-3, HPMC
9004-67-5, Methyl cellulose 17465-86-0, γ -Cyclodextrin
31465-25-5D, 1-Butanesulfonic acid, 4-hydroxy-, monosodium salt, ether
with β -cyclodextrin 104723-60-6, Maltosyl- β -cyclodextrin
107035-66-5, Dimaltosyl- β -cyclodextrin
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)

(methods to enhance the complexation efficiency of cyclodextrins)

IT 107035-66-5, Dimaltosyl- β -cyclodextrin

RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)

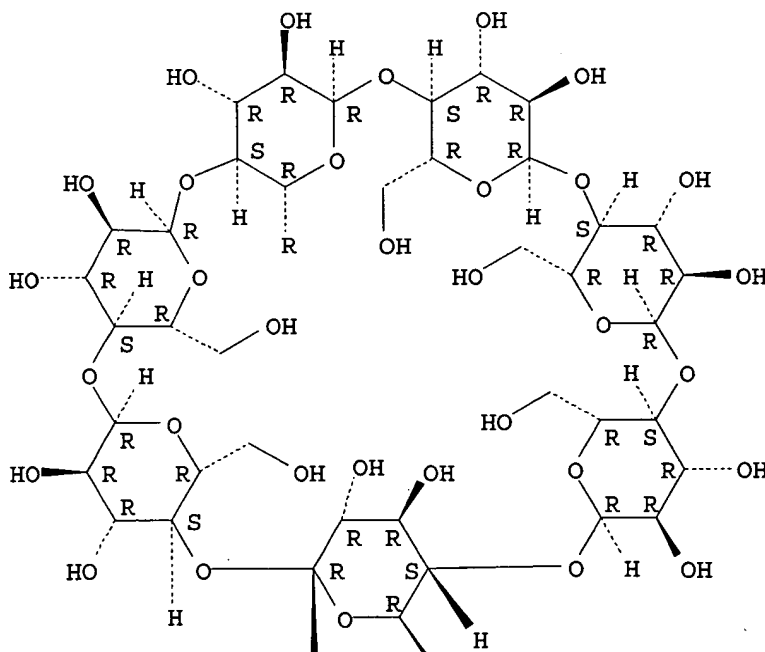
(methods to enhance the complexation efficiency of cyclodextrins)

RN 107035-66-5 HCAPLUS

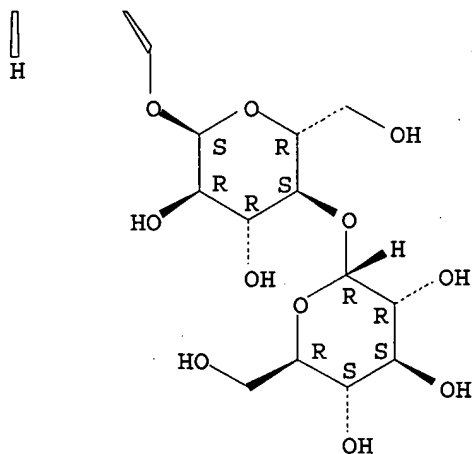
CN β -Cyclodextrin, O- α -D-glucopyranosyl-(1 \rightarrow 4)-O- α -D-glucopyranosyl-(1 \rightarrow 6A)-O-[O- α -D-glucopyranosyl-(1 \rightarrow 4)- α -D-glucopyranosyl-(1 \rightarrow 6D)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

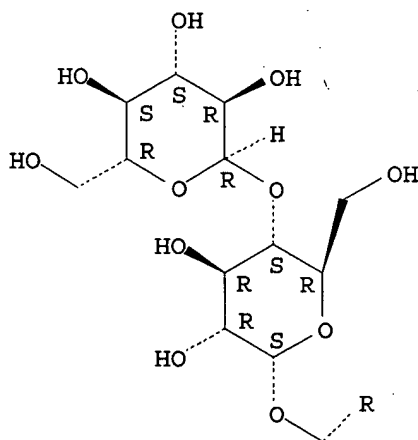
PAGE 1-A



PAGE 2-A



PAGE 3-A



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1995:336115 HCAPLUS
 DOCUMENT NUMBER: 122:240230
 TITLE: Molecular recognition by cyclodextrin dimers
 AUTHOR(S): Breslow, Ronald; Halfon, Sherin; Zhang, Biliang
 CORPORATE SOURCE: Dep. of Chemistry, Columbia Univ., New York, NY, 10027, USA
 SOURCE: Tetrahedron (1995), 51(2), 377-88
 CODEN: TETRAB; ISSN: 0040-4020
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Cyclodextrin dimers strongly bind substrates with the correct geometry in water solution. Studies with antihydrophobic agents help clarify the factors involved.

CC 33-5 (Carbohydrates)

IT **Polymers**, preparation

RL: SPN (Synthetic preparation); PREP (Preparation)
(cyclodextrin group-containing, cyclodextrin dimers; mol. recognition by cyclodextrin dimers)

IT 6240-11-5, 2-(1-Adamantyl)ethanol 94827-13-1 **96761-41-0**
123290-02-8 123307-79-9 130860-88-7 152310-62-8 162158-20-5
162158-21-6 162190-57-0 162190-60-5

RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(mol. recognition by cyclodextrin dimers)

IT **96761-41-0**

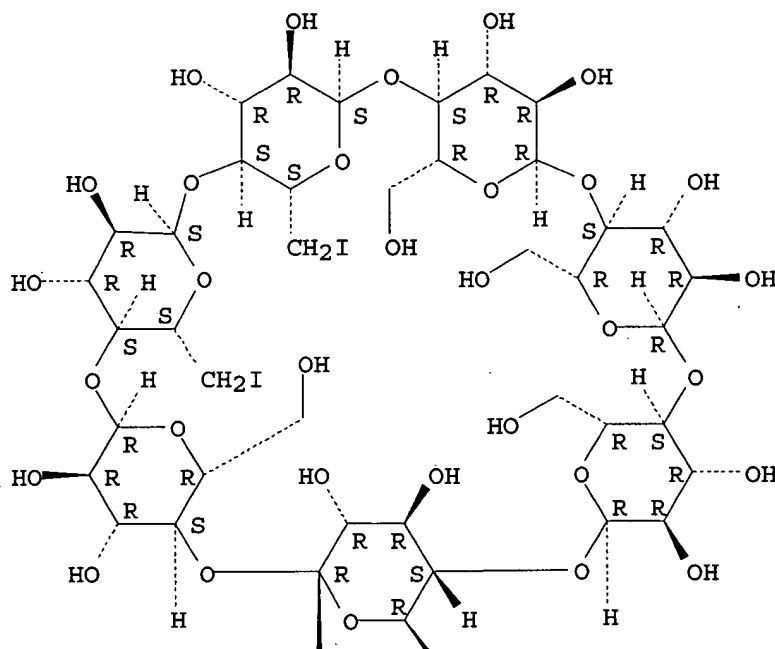
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(mol. recognition by cyclodextrin dimers)

RN 96761-41-0 HCAPLUS

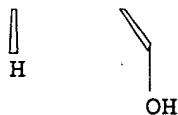
CN β -Cyclodextrin, 6A,6B-dideoxy-6A,6B-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



L55 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1991:559565 HCAPLUS

DOCUMENT NUMBER: 115:159565

TITLE: Characterization of five isomers of branched cyclomaltoheptaose (β CD) having degree of polymerization (d.p.) = 9: reinvestigation of three positional isomers of diglucosyl- β CD

AUTHOR(S): Koizumi, Kyoko; Tanimoto, Toshiko; Okada, Yasuyo; Nakanishi, Noriko; Kato, Nagako; Takagi, Yosuke; Hashimoto, Hitoshi

CORPORATE SOURCE: Fac. Pharm. Sci., Mukogawa Women's Univ., Nishinomiya, 663, Japan

SOURCE: Carbohydrate Research (1991), 215(1), 127-36
CODEN: CRBRAT; ISSN: 0008-6215

DOCUMENT TYPE: Journal

LANGUAGE: English

AB It has been confirmed by methylation analyses and chemical syntheses that three isomers of branched cyclomaltoheptaose isolated from the mother liquors of a large-scale preparation of β -CD with *Bacillus ohbensis* cyclomaltodextrin glucanotransferase are 61,64-di-O-(α -D-glucopyranosyl)-cyclomaltoheptaose, 61,63-di-O-(α -D-glucopyranosyl)-cyclomaltoheptaose, and 6-O-(α -isomaltosyl)-cyclomaltoheptaose instead of 61,62-di-O-(α -D-glucopyranosyl)-cyclomaltoheptaose (I), which was erroneously characterized in an earlier paper. I has been newly isolated from a glucosyl- β -CD mixture prepared by hydrolysis with glucoamylase of a maltosyl- β -CD mixture, synthesized from maltose and β -CD through the reverse action of pullulanase. 6-O-(α -Maltosyl)-cyclomaltoheptaose was prepared by the reverse action of hydrolytic enzymes.

CC 33-5 (Carbohydrates)

IT 130925-49-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(acetylation and desilylation of)

IT 130925-49-4

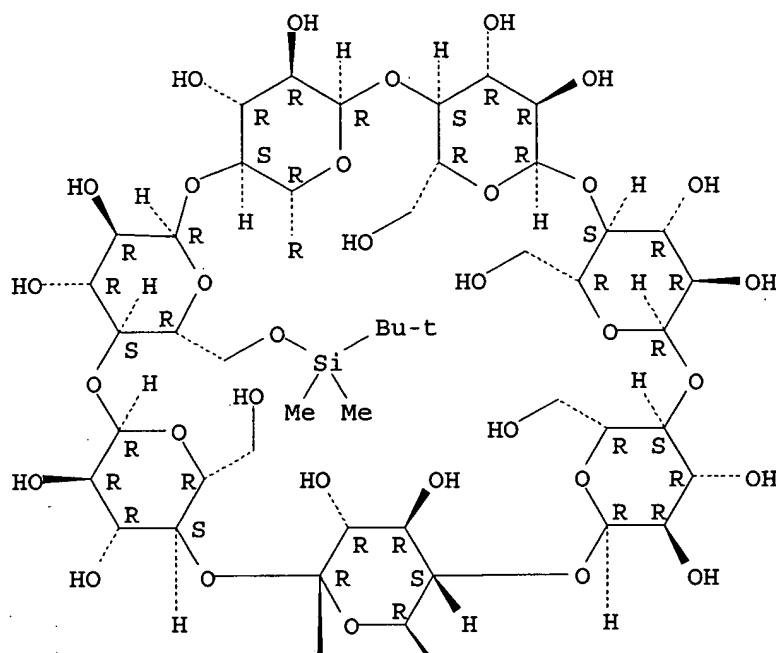
RL: RCT (Reactant); RACT (Reactant or reagent)
(acetylation and desilylation of)

RN 130925-49-4 HCAPLUS

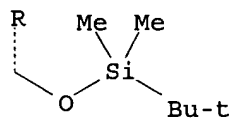
CN β -Cyclodextrin, 6A,6B-bis-O-[(1,1-dimethylethyl)dimethylsilyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



cyclodextrin reaction sites + text (linear polymer)

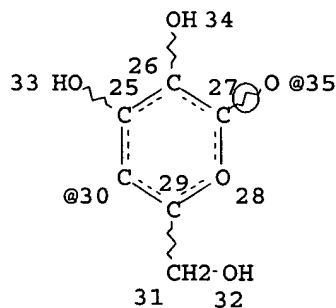
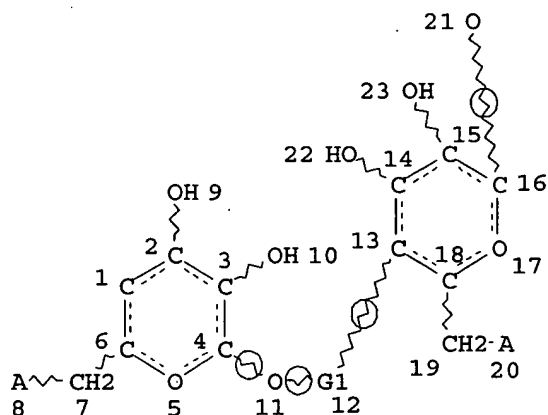
Crane 09/339,818

June 23, 2004

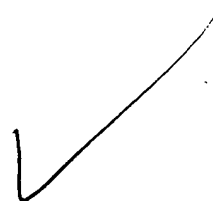
=> d que 131

L4

STR



3/8



REP G1=(0-3) 30-11 35-13

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

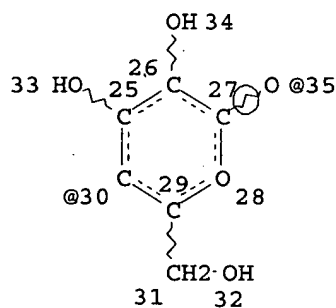
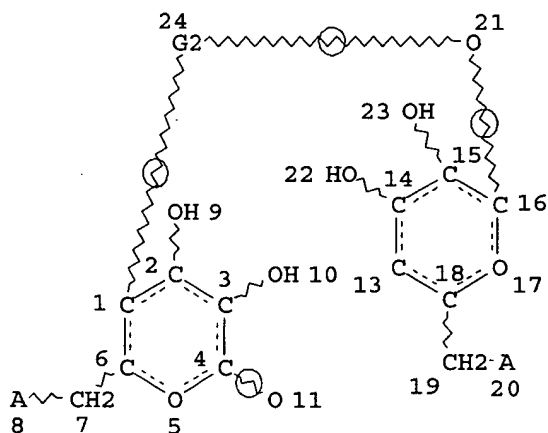
NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE

L6 21339 SEA FILE=REGISTRY SSS FUL L4

L7

STR



REP G2=(2-6) 30-21 35-1

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

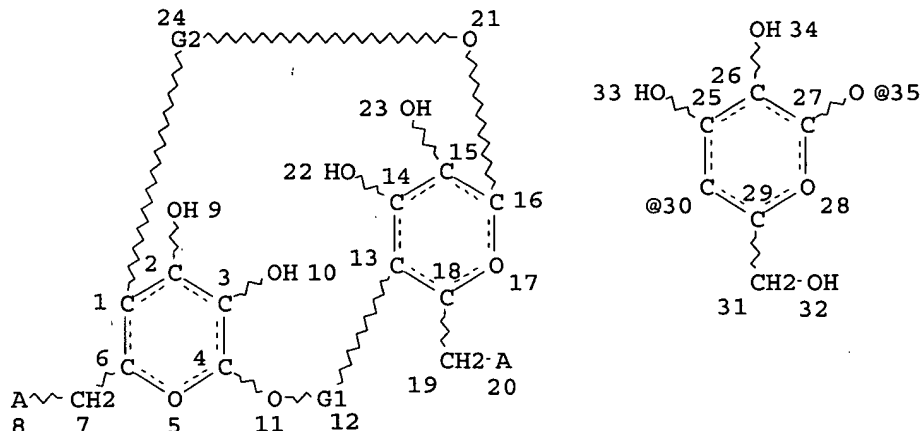
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE

L9 19801 SEA FILE=REGISTRY SUB=L6 SSS FUL L7
L11 STR

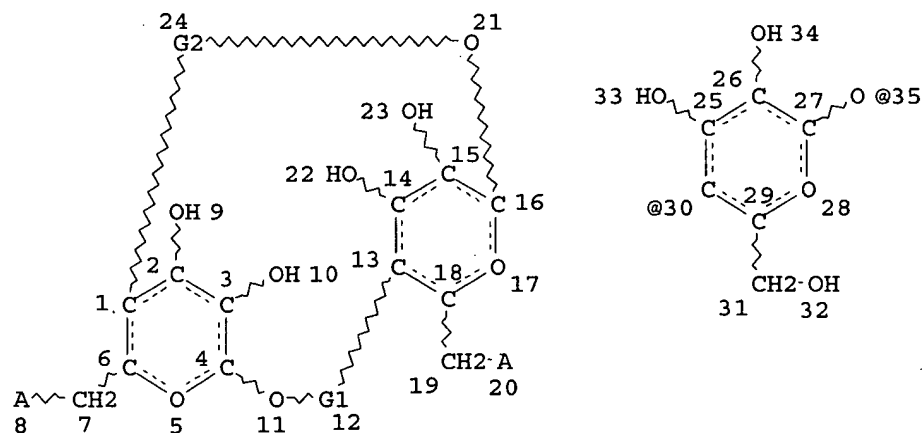


REP G1=(0-3) 30-11 35-13
REP G2=(2-4) 30-21 35-1
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE

L13 17536 SEA FILE=REGISTRY SUB=L9 SSS FUL L11
L14 STR



REP G1=(0-3) 30-11 35-13
REP G2=(5-6) 30-21 35-1
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

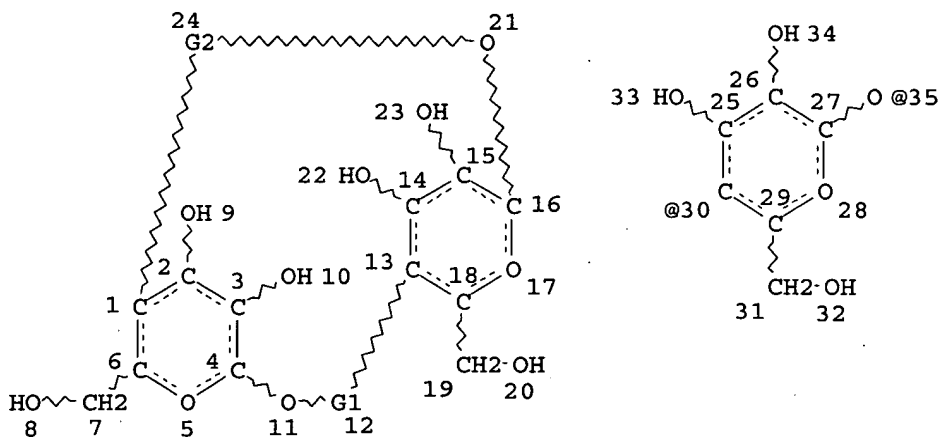
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE

L15 13536 SEA FILE=REGISTRY SUB=L9 SSS FUL L14

L16 17980 SEA FILE=REGISTRY ABB=ON PLU=ON L13 OR L15

L17 STR



REP G1=(0-3) 30-11 35-13

REP G2=(2-4) 30-21 35-1

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

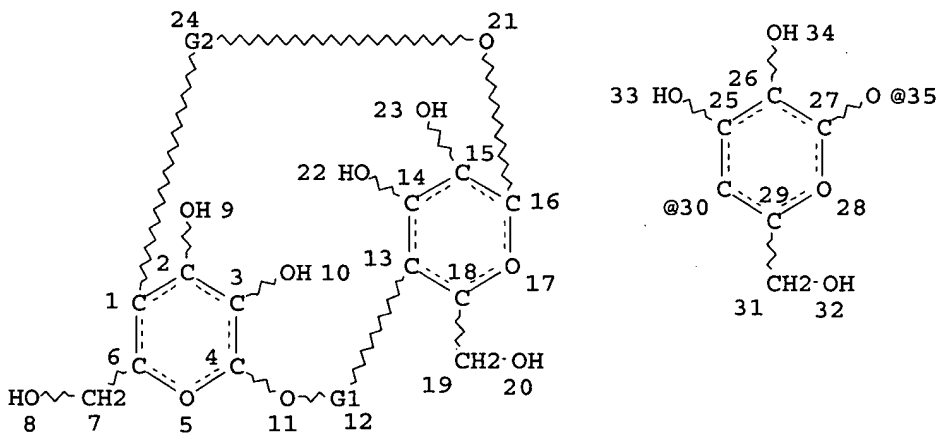
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE

L18 12481 SEA FILE=REGISTRY SUB=L9 SSS FUL L17

L19 STR



REP G1=(0-3) 30-11 35-13

REP G2=(5-6) 30-21 35-1

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 35

STEREO ATTRIBUTES: NONE

L20 9233 SEA FILE=REGISTRY SUB=L9 SSS FUL L19
L21 12511 SEA FILE=REGISTRY ABB=ON PLU=ON L18 OR L20
L22 5469 SEA FILE=REGISTRY ABB=ON PLU=ON L16 NOT L21
L29 806 SEA FILE=HCAPLUS ABB=ON PLU=ON L22(L) (RACT OR RCT OR RGT)/RL

L31 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND LINEAR?(3A)?POLYMER?

=>d 131 ibib abs hitind hitstr 1-5.

L31 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:789443 HCAPLUS

DOCUMENT NUMBER: 140:16882

TITLE: Supra-Molecular Self-Assemblies of
β-Cyclodextrins with Aromatic Tethers: Factors
Governing the Helical Columnar versus Linear Channel
Super-Structures

AUTHOR(S): Liu, Yu; Fan, Zhi; Zhang, Heng-Yi; Yang, Ying-Wei;
Ding, Fei; Liu, Shuang-Xi; Wu, Xue; Wada, Takehiko;
Inoue, Yoshihisa

CORPORATE SOURCE: Department of Chemistry, State Key Laboratory of
Elemento-Organic Chemistry, Nankai University,
Tianjin, 300071, Peop. Rep. China
SOURCE: Journal of Organic Chemistry (2003), 68(22), 8345-8352
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:16882

AB A series of 6-O-(p-substituted phenyl)-modified β-cyclodextrin
derivs., i.e., 6-O-(4-bromophenyl)-β-CD (1), 6-O-(4-nitrophenyl)-
β-CD (2), 6-O-(4-formylphenyl)-β-CD (3), 6-phenylselenyl-6-deoxy-
β-CD (4), and 6-O-(4-hydroxybenzoyl)-β-CD (5), were synthesized,
and their inclusion complexation behavior in aqueous solution and

self-assembling

behavior in the solid state were comparatively studied by NMR
spectroscopy, micro-calorimetry, crystallog., and scanning tunneling
microscopy. Interestingly, (seleno)ethers 1-4 and ester 5 displayed
distinctly different self-assembling behavior in the solid state,
affording a successively threading head-to-tail polymeric helical
structure for the (seleno)ethers or a mutually penetrating tail-to-tail
dimeric columnar channel structure for the ester. Combining the present
and previous structures reported for the relevant β-CD derivs., we
further deduce that the pivot hetero-atom, through which the aromatic
substituent is tethered to β-CD, plays a critical role in determining the
helix structure, endowing the 2-fold and 4-fold axes to the N/O- and
S/Se-pivoted β-CD aggregates, resp. This means that one can control
the self-assembling orientation, alignment, and helicity in the solid
state by finely tuning the pivot atom and the tether length. Further NMR
and calorimetric studies on the self-assembling behavior in aqueous solution
revealed that the dimerization step is the key to the formation of
linear polymeric supramol. architecture, which is driven
by favorable entropic contributions.

CC 33-4 (Carbohydrates)

Section cross-reference(s): 22, 69, 75

IT 140874-31-3

RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)

(preparation, inclusion reaction, and supramol. self-assemblies of β -cyclodextrins with aromatic tethers and factors governing helical columnar vs. linear channel super-structures)

IT 500757-70-0P 629652-79-5P 629652-80-8P
629652-81-9P

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, inclusion reaction, and supramol. self-assemblies of β -cyclodextrins with aromatic tethers and factors governing helical columnar vs. linear channel super-structures)

IT 99-96-7, 4-Hydroxybenzoic acid, reactions 100-02-7, 4-Nitrophenol, reactions 106-41-2, 4-Bromophenol 123-08-0, 4-Hydroxybenzaldehyde 7585-39-9, β -Cyclodextrin 67217-55-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation, inclusion reaction, and supramol. self-assemblies of β -cyclodextrins with aromatic tethers and factors governing helical columnar vs. linear channel super-structures)

IT 140874-31-3

RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)

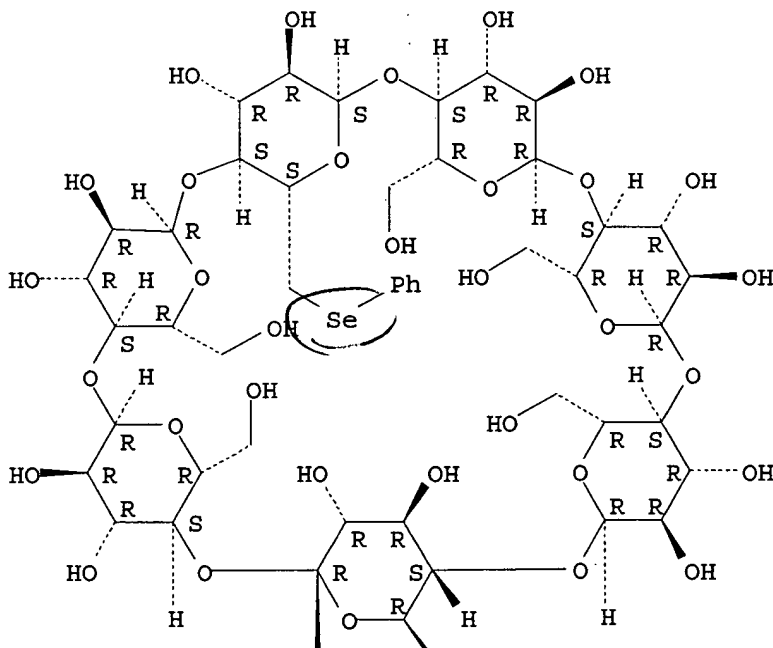
(preparation, inclusion reaction, and supramol. self-assemblies of β -cyclodextrins with aromatic tethers and factors governing helical columnar vs. linear channel super-structures)

RN 140874-31-3 HCAPLUS

CN β -Cyclodextrin, 6A-Se-phenyl-6A-seleno- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT 500757-70-0P 629652-79-5P 629652-80-8P
629652-81-9P

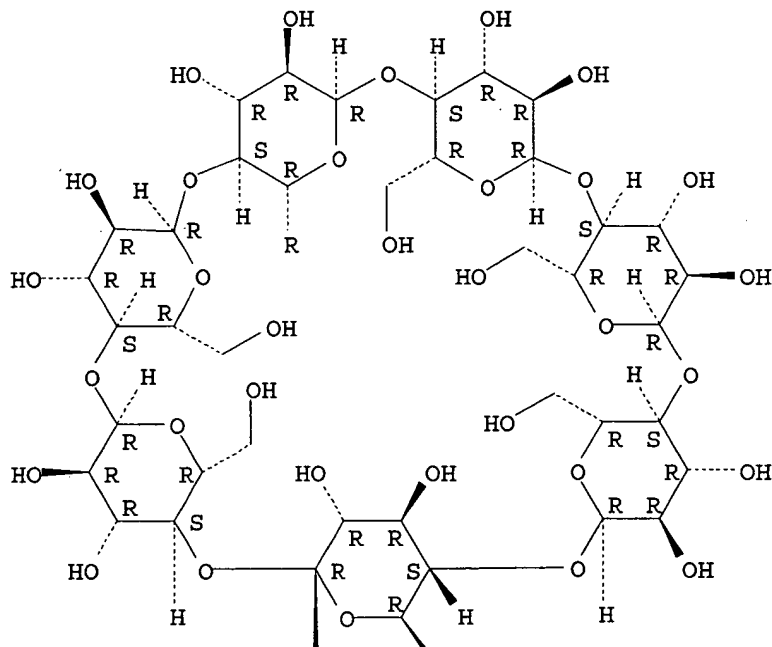
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation, inclusion reaction, and supramol. self-assemblies of β -cyclodextrins with aromatic tethers and factors governing helical columnar vs. linear channel super-structures)

RN 500757-70-0 HCAPLUS

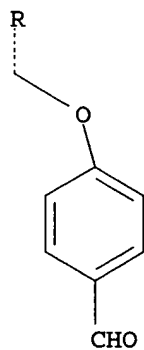
CN β -Cyclodextrin, 6A-O-(4-formylphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

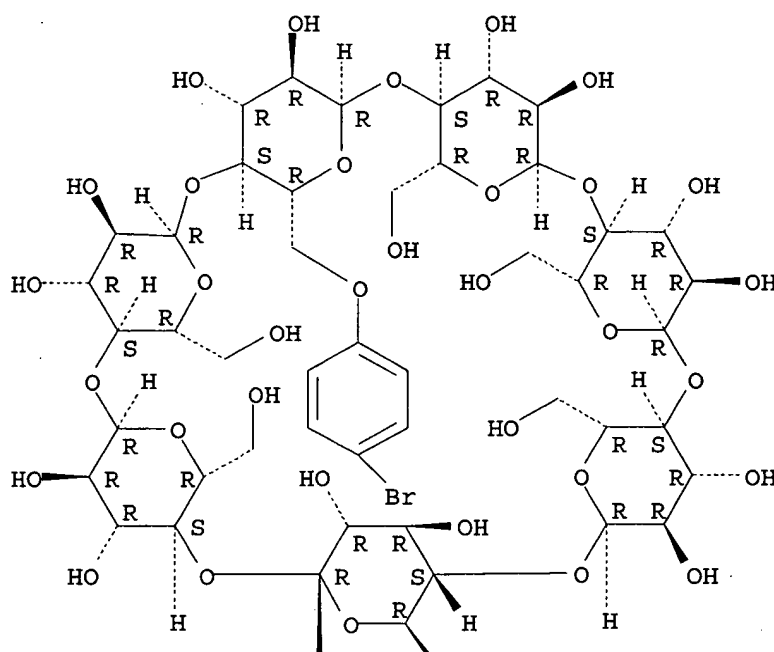


RN 629652-79-5 HCAPLUS

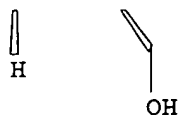
CN β -Cyclodextrin, 6A-O-(4-bromophenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

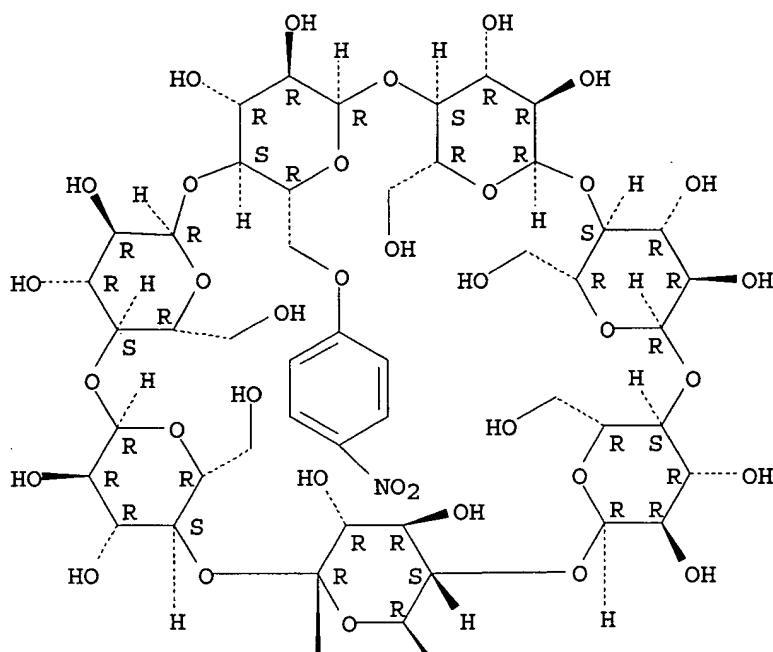


RN 629652-80-8 HCAPLUS

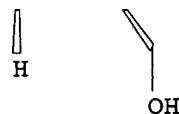
CN β -Cyclodextrin, 6A-O-(4-nitrophenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

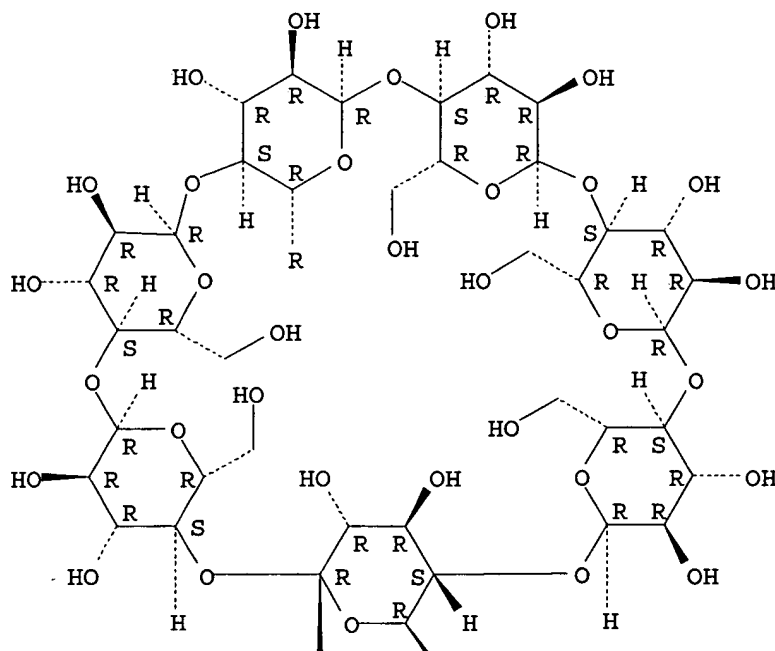


RN 629652-81-9 HCAPLUS

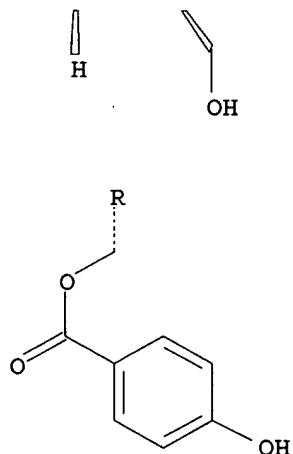
CN β -Cyclodextrin, 6A-(4-hydroxybenzoate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT 67217-55-4

RL: RCT (Reactant); RACT (Reactant or reagent)

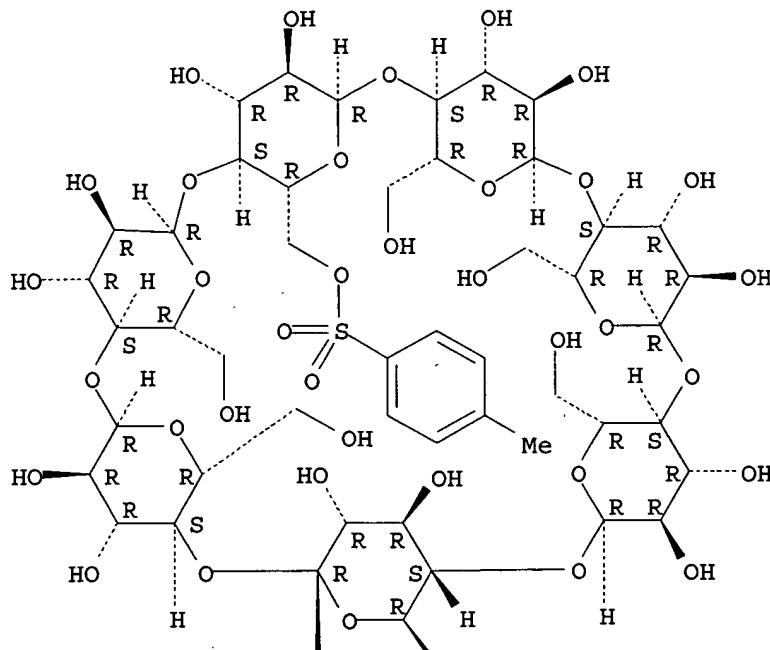
(preparation, inclusion reaction, and supramol. self-assemblies of β -cyclodextrins with aromatic tethers and factors governing helical columnar vs. linear channel super-structures)

RN 67217-55-4 HCAPLUS

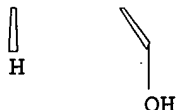
CN β -Cyclodextrin, 6A-(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:666072 HCAPLUS

DOCUMENT NUMBER: 139:328131

TITLE: Synthesis of Linear, β -Cyclodextrin-Based Polymers and Their Camptothecin Conjugates

AUTHOR(S): Cheng, Jianjun; Khin, Kay T.; Jensen, Gregory S.; Liu, Aijie; Davis, Mark E.

CORPORATE SOURCE: Insert Therapeutics, Inc., Pasadena, CA, 91107, USA

SOURCE: Bioconjugate Chemistry (2003), 14(5), 1007-1017

CODEN: BCCHE5; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 6A,6D-Bis-(2-amino-2-carboxylethylthio)-6A,6D-dideoxy- β -cyclodextrin 1, a diamino acid derivative of β -cyclodextrin, is synthesized and condensed with difunctionalized PEG comonomers to give linear, high mol. weight (M_w over 50 kDa) β -cyclodextrin-based polymers (2-4) with pendant functionality (carboxylate). 2-4 Are all highly soluble in aqueous solns.

(over

70M

200 mg/mL). 20-O-trifluoroglycinylcampthothecin, 5a, and 20-O-trifluoroglycinylglycinylglycinylcampthothecin, 5b, are synthesized and conjugated to 2 to give polymer-campthothecin (CPT) prodrugs. The solubility of CPT is increased by more than three orders of magnitude when it is conjugated to 2. The rates of CPT release from the conjugates HGGG6 (high mol. weight polymer (Mw 97 kDa), glyglygly linker and 6 wt % CPT loading) and HG6 (high MW polymer (Mw 97 kDa), gly linker and 6 wt % CPT loading) in either mouse or human plasma are dramatically accelerated over the rates of pure hydrolysis at pH = 7.4, indicating the presence of enzymic cleavage as a rate-determining step at this pH in the release of the CPT. The pH of aqueous solution has a large effect on hydrolysis rate of CPT from HGGG6 and HG6; the lower the pH, the slower the rate in the range at $4.1 \leq \text{pH} \leq 13.1$. The IC₅₀'s of polymer 2e, CPT, and the CPT conjugates HG6 and HGGG6 are found to be cell-line dependent with LS174T, HT29, A2780, and PC3 cells using in vitro MTT assays. The parent polymer 2e has very low toxicity to all cultured cells tested.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 35

IT Human

(A2780 cell line; synthesis of **linear**, β -Cyclodextrin-based **polymers** and their campthothecin conjugates)

IT Animal cell line

(HT-29; synthesis of **linear**, β -Cyclodextrin-based **polymers** and their campthothecin conjugates)

IT Animal cell line

(LS174T; synthesis of **linear**, β -Cyclodextrin-based **polymers** and their campthothecin conjugates)

IT Animal cell line

(PC-3; synthesis of **linear**, β -Cyclodextrin-based **polymers** and their campthothecin conjugates)

IT Polyoxyalkylenes, preparation

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(polyamide-; synthesis of **linear**, β -Cyclodextrin-based **polymers** and their campthothecin conjugates)

IT Polyamides, preparation

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(polyoxyalkylene-; synthesis of **linear**, β -Cyclodextrin-based **polymers** and their campthothecin conjugates)

IT Drug delivery systems

(prodrugs; synthesis of **linear**, β -Cyclodextrin-based **polymers** and their campthothecin conjugates)

IT Antitumor agents

Dissolution

Hydrolysis

Stability

(synthesis of **linear**, β -Cyclodextrin-based **polymers** and their campthothecin conjugates)

IT 204133-74-4DP, reaction products with cyclodextrin polyamides

362496-98-8DP, reaction products with cyclodextrin polyamides

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of **linear**, β -Cyclodextrin-based **polymers** and their campthothecin conjugates)

IT 7689-03-4, 20(S)-Campthothecin

RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(synthesis of **linear**, β -Cyclodextrin-based
polymers and their camptothecin conjugates)
IT 614744-05-7DP, camptothecin conjugate derivs. 614744-06-8P
614744-08-0P 614744-10-4P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic
preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of **linear**, β -Cyclodextrin-based
polymers and their camptothecin conjugates)
IT 52-90-4, L-Cysteine, reactions 4530-20-5 28320-73-2 34079-22-6
123502-57-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of **linear**, β -Cyclodextrin-based
polymers and their camptothecin conjugates)
IT 76700-72-6P 204133-74-4P 362496-98-8P 614744-04-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(synthesis of **linear**, β -Cyclodextrin-based
polymers and their camptothecin conjugates)
IT 614744-05-7DP, camptothecin conjugate derivs. 614744-06-8P
614744-08-0P 614744-10-4P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic
preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of **linear**, β -Cyclodextrin-based
polymers and their camptothecin conjugates)
RN 614744-05-7 HCAPLUS
CN L-Cysteine, S,S'-(6A,6D-dideoxy- β -cyclodextrin-6A,6D-diyl)bis-,
polymer with α -[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]-
 ω -[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropoxy]poly(oxy-1,2-
ethanediyl) (9CI) (CA INDEX NAME)

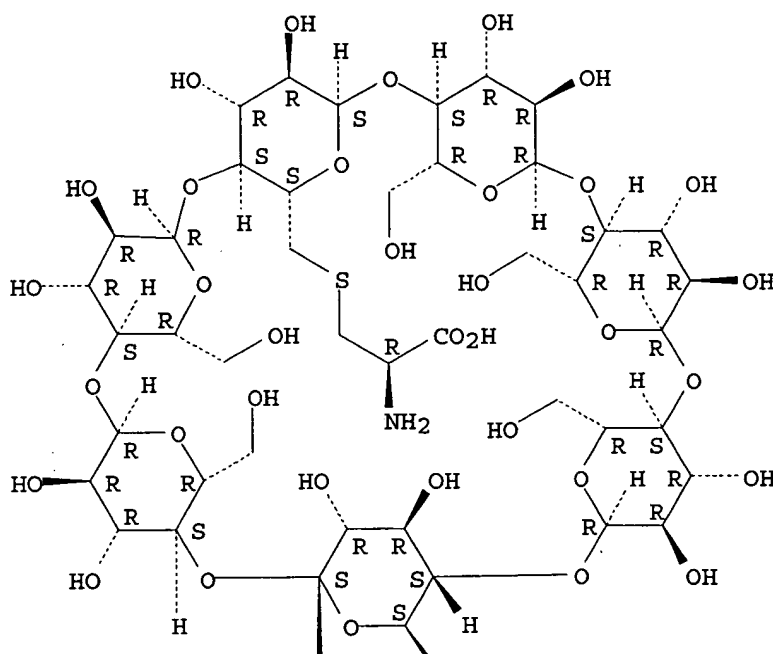
CM 1

CRN 614744-04-6

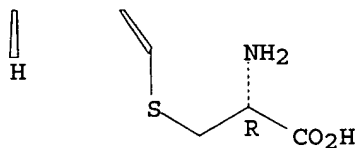
CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



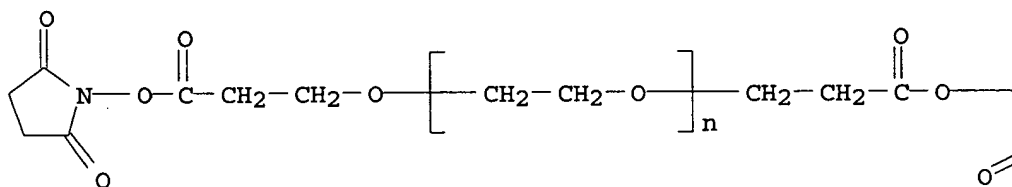
CM 2

CRN 123502-57-8

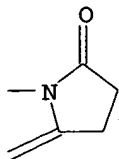
CMF (C2 H4 O)_n C14 H16 N2 O9

CCI PMS

PAGE 1-A



PAGE 1-B



RN 614744-06-8 HCAPLUS
 CN L-Cysteine, S,S'-(6A,6D-dideoxy- β -cyclodextrin-6A,6D-diyl)bis-,
 polymer with α -[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutyl]-
 ω -[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]poly(oxy-1,2-
 ethanediyl) (9CI) (CA INDEX NAME)

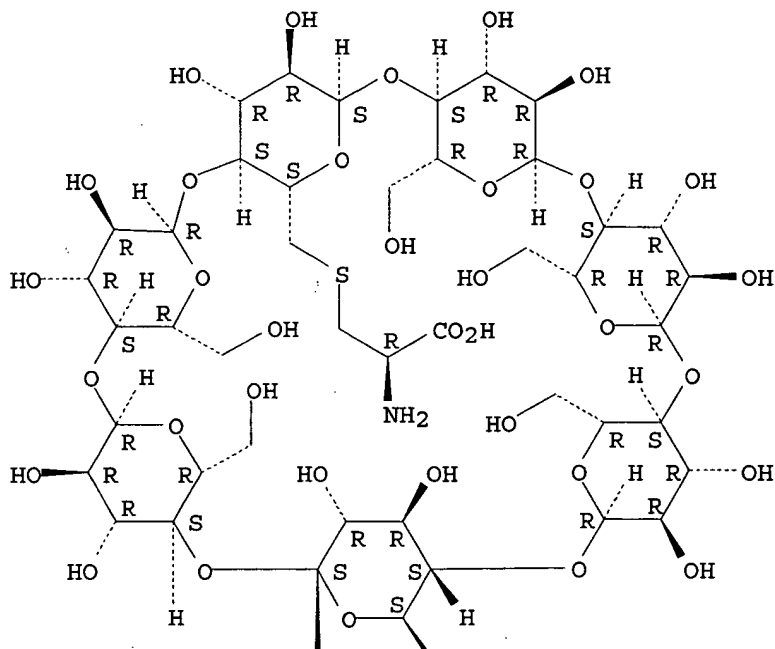
CM 1

CRN 614744-04-6

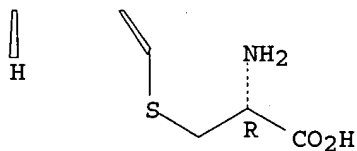
CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

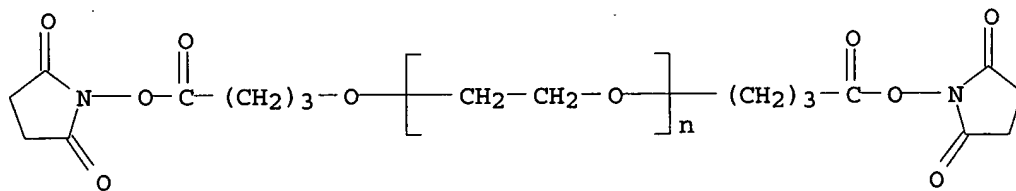


CM 2

CRN 159194-63-5

CMF (C2 H4 O)_n C16 H20 N2 O9

CCI PMS



RN 614744-08-0 HCAPLUS

CN L-Cysteine, S,S'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis-,
polymer with α-[(1H-benzotriazol-1-yloxy) carbonyl]-ω-[[1H-
benzotriazol-1-yloxy) carbonyl]oxy]poly(oxy-1,2-ethanediyl) (9CI) (CA
INDEX NAME)

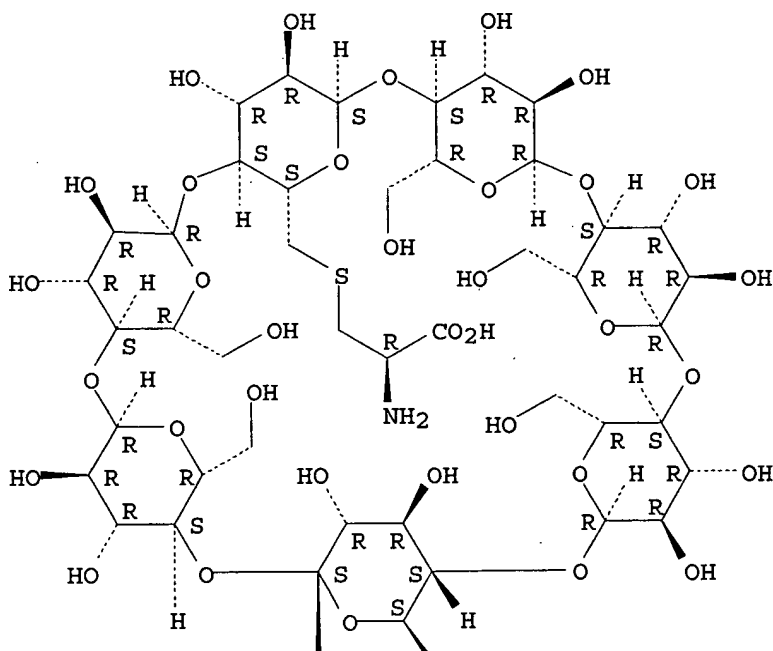
CM 1

CRN 614744-04-6

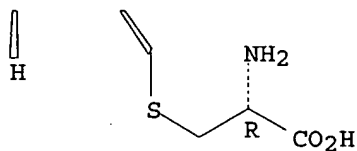
CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

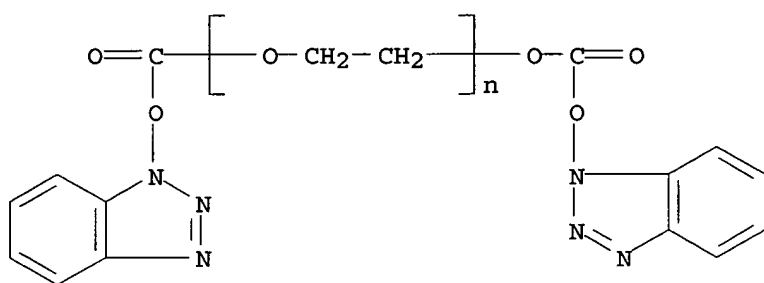


CM 2

CRN 178676-34-1

CMF (C2 H4 O)_n C14 H8 N6 O5

CCI PMS



RN 614744-10-4 HCAPLUS

CN L-Cysteine, S,S'-(6A,6D-dideoxy-β-cyclodextrin-6A,6D-diyl)bis-,
 polymer with α-[(4-nitrophenoxy)carbonyl]-ω-[[4-nitrophenoxy)carbonyl]oxy]poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

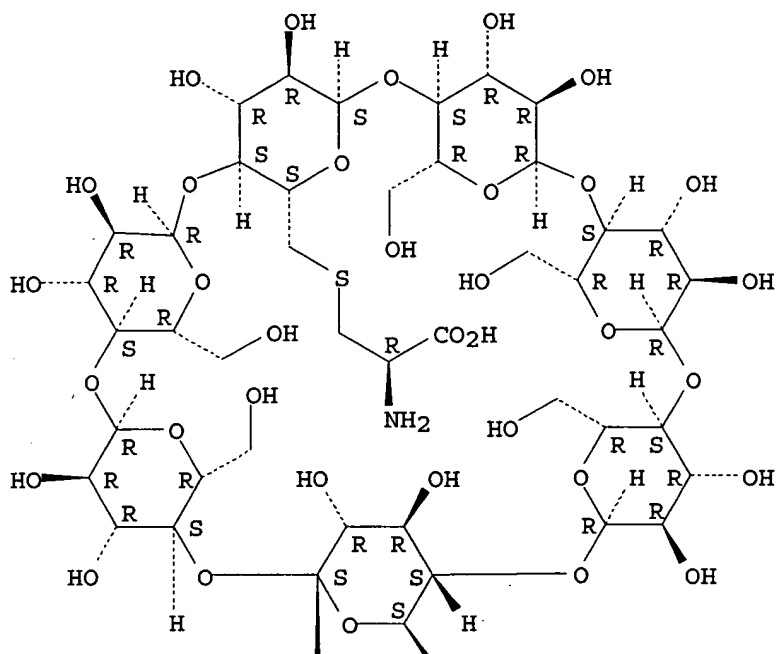
CM 1

CRN 614744-04-6

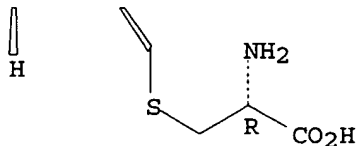
CMF C48 H80 N2 O37 S2

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

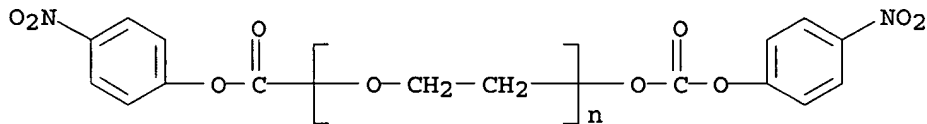


CM 2

CRN 150673-50-0

CMF (C2 H4 O)_n C14 H8 N2 O9

CCI PMS



IT 76700-72-6P 614744-04-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

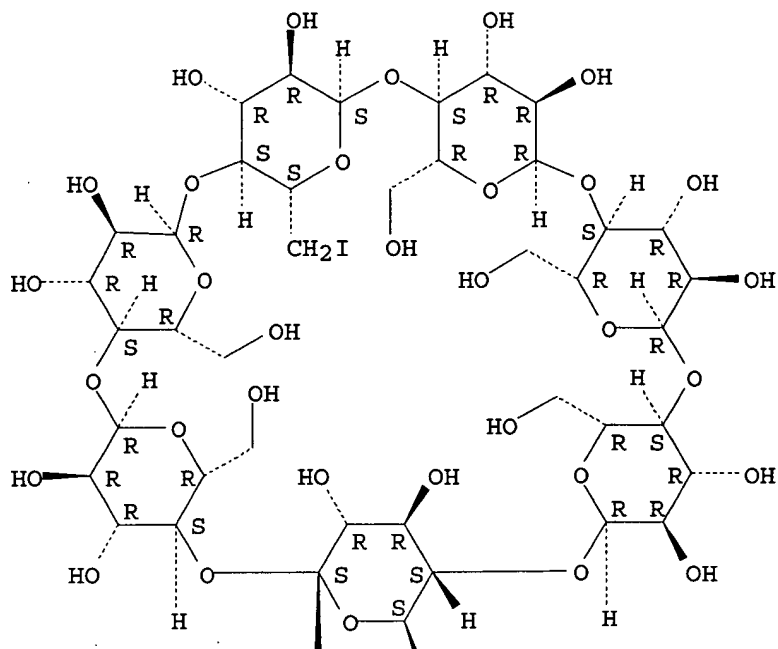
(synthesis of linear, β -Cyclodextrin-based polymers and their camptothecin conjugates)

RN 76700-72-6 HCAPLUS

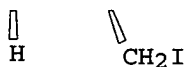
CN β -Cyclodextrin, 6A,6D-dideoxy-6A,6D-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

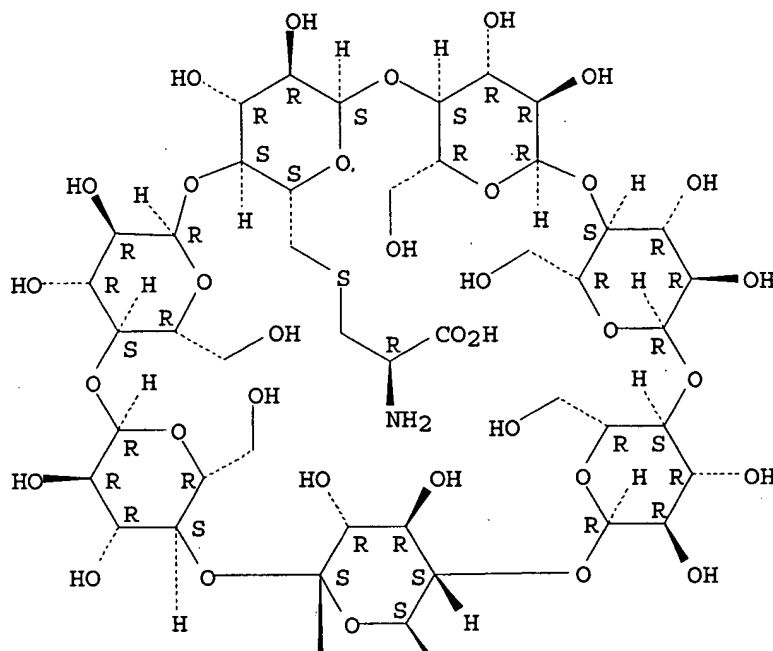


RN 614744-04-6 HCAPLUS

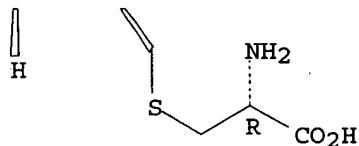
CN L-Cysteine, S,S'-(6A,6D-dideoxy- β -cyclodextrin-6A,6D-diyl)bis- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:167523 HCAPLUS

DOCUMENT NUMBER: 138:207334

TITLE: Linear tube-shaped nitrated cyclodextrin polymers for encapsulation of nitramine explosives

INVENTOR(S): Ruebner, Anja; Statton, Gary L.; Consaga, John P.

PATENT ASSIGNEE(S): Mach I, Inc., USA

SOURCE: U.S., 10 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6527887	B1	20030304	US 2002-52430	20020118
PRIORITY APPLN. INFO.:			US 2002-52430	20020118

AB Linear tube-shaped nitrated cyclodextrin polymers, with mol. wts. 2000-50,000 and containing 10-20% nitrogen, are prepared from α -, β -, and γ -cyclodextrin starting materials that are connected by bifunctional linking groups, of general structures -O-X-(A)-Y-O- (X and Y are independently -CH-, a chain of -CH₂- or Ph groups, and A = H, OH, NH₂, CO₂H, or -CH₃) and -[X-Z(X_n-Y)_m]_p (X = -CH₂-, Z = -CH-, Y = NH₂, CO₂H, and OH; n = 0-1, m = 1, and p = 20-200). The cyclodextrins are bound to the polymer backbone by a secondary amine, urethane, ester, or ether bonds, and they can encapsulate conventional explosives (e.g., RDX or HMX) to form desensitized explosives. Synthesis is preferably carried out using a supported water-swallowable polystyrene-based resin.

IC ICM C06B025-02
ICS C08G063-91

NCL 149108000; 525054200; 525054300; 525054420; 525063000; 525066000;
524081000; 149088000; 149108600; 149108800

CC 50-2 (Propellants and Explosives)
Section cross-reference(s): 35, 38

IT Nitration
(in liquid carbon dioxide, of cyclodextrin **polymers**;
linear tube-shaped nitrated cyclodextrin polymers for
encapsulation of nitramine explosives)

IT 10102-03-1, Dinitrogen pentoxide
RL: RCT (Reactant); RACT (Reactant or reagent)
(nitrating agent, for cyclodextrin **polymers**; **linear**
tube-shaped nitrated cyclodextrin polymers for encapsulation of
nitramine explosives)

IT 97227-33-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(synthesis and poly(allylamine) reaction with; in synthesis of linear
tube-shaped nitrated cyclodextrin polymers for encapsulation of
nitramine explosives)

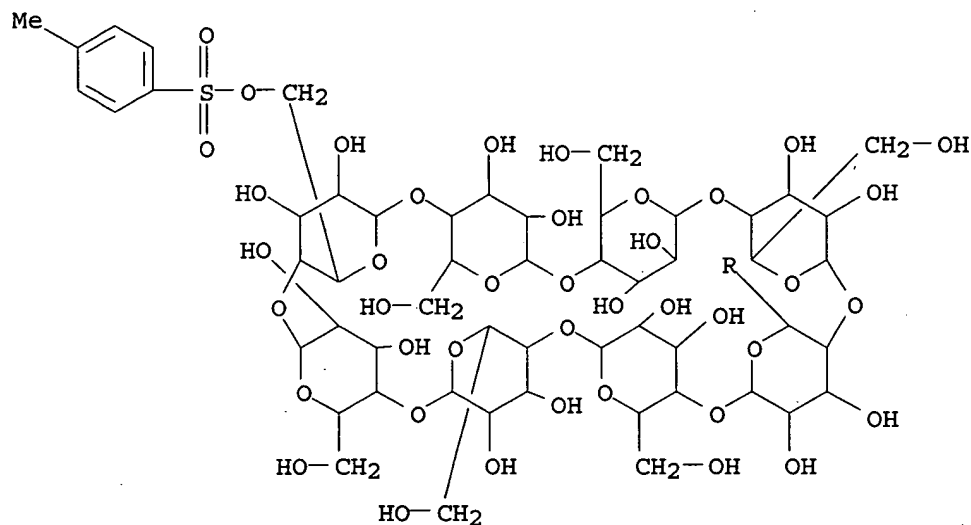
IT 25916-38-5DP, α -Cyclodextrin-epichlorohydrin copolymer,
borohydride-reduced, nitrated 30551-89-4DP, Poly(allyl amine), compds.
with 6-tolylsulfonyl-6-deoxy-2-cyclodextrin 97227-33-3DP, compds. with
poly(allyl amine) 350811-56-2P, α -Cyclodextrin-epichlorohydrin
copolymer, nitrate 500314-75-0P, Cyclodextrin-4,4'-MDI
copolymer, nitrate
RL: SPN (Synthetic preparation); TEM (Technical or engineered material
use); PREP (Preparation); USES (Uses)
(synthesis of **linear** tube-shaped nitrated cyclodextrin
polymers for encapsulation of nitramine explosives)

IT 97227-33-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(synthesis and poly(allylamine) reaction with; in synthesis of linear
tube-shaped nitrated cyclodextrin polymers for encapsulation of
nitramine explosives)

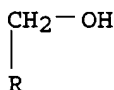
RN 97227-33-3 HCAPLUS

CN γ -Cyclodextrin, 6A-(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31. ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:401687 HCAPLUS

DOCUMENT NUMBER: 133:48948

TITLE: Supramolecular complexes containing therapeutic agents

INVENTOR(S): Davis, Mark E.; Gonzalez, Hector; Hwang, Suzie

PATENT ASSIGNEE(S): California Institute of Technology, USA

SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

Appl's and work

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000033885	A1	20000615	WO 1999-US28547	19991203
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1133318	A1	20010919	EP 1999-965967	19991203

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

JP 2002531530 T2 20020924 JP 2000-586375 19991203

PRIORITY APPLN. INFO.: US 1998-110847P P 19981204

US 1999-127856P P 19990405

WO 1999-US28547 W 19991203

AB A method of preparing a supramol. complex containing at least one therapeutic agent and a multi-dimensional polymer network is described. A supramol. complex prepared by a method of the invention is described. A method of treatment by administering a therapeutically effective amount of a supramol. complex of the invention is also described. Such a supramol. complex may be used as a delivery vehicle for various therapeutic agents. The **polymers** include **linear** or branched polyethyleneimine and cyclodextrin derivs.

IC ICM A61K047-48

ICS A61K031-335; A61K031-70

CC 63-6 (Pharmaceuticals)

IT 9002-98-6DP, Polyethylenimine, reaction product with β -cyclodextrinethiol and functionalized PEG 25322-68-3DP, PEG, reaction product with β -cyclodextrinethiol and polyethylenimine
29390-66-7P 35625-91-3P 39927-08-7P 52539-19-2P
67217-55-4P 73499-21-5P 76700-72-6P
81644-55-5DP, reaction product with functionalized PEG and polyethylenimine 81644-55-5P 98126-99-9P
101652-40-8P 254912-03-3P 254912-04-4P
254912-05-5DP, oxidized 254912-05-5P
254912-07-7P 254912-09-9P 275354-50-2P
275354-52-4DP, reaction products with DNA 275354-53-5P
275354-54-6P 275354-55-7P 275354-57-9P
275354-58-0P 275354-59-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(preparation of supramol. complexes containing therapeutic agents)

IT 29390-66-7P 67217-55-4P 76700-72-6P

81644-55-5DP, reaction product with functionalized PEG and polyethylenimine 81644-55-5P 98126-99-9P

101652-40-8P 254912-03-3P 254912-04-4P

254912-05-5DP, oxidized 254912-05-5P

254912-07-7P 254912-09-9P 275354-52-4DP,

reaction products with DNA 275354-53-5P 275354-54-6P

275354-55-7P 275354-57-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

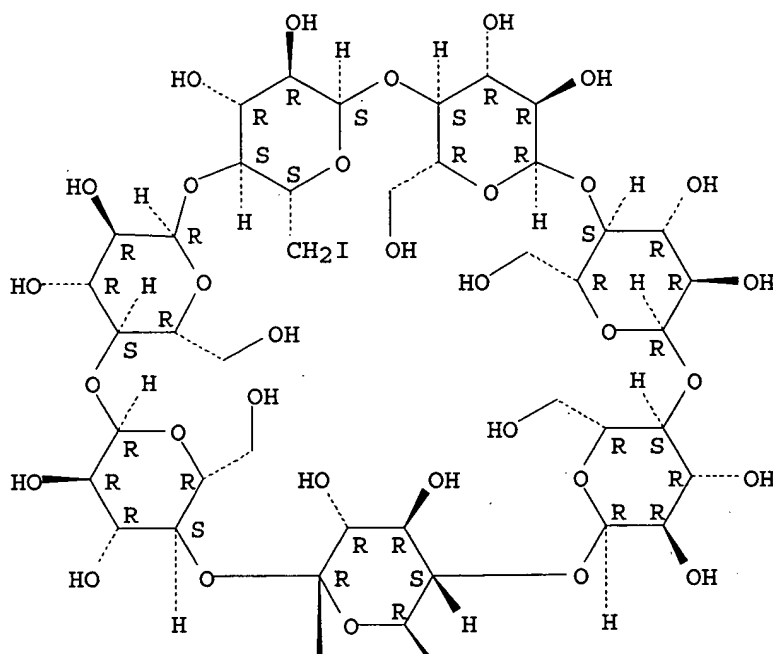
(preparation of supramol. complexes containing therapeutic agents)

RN 29390-66-7 HCAPLUS

CN β -Cyclodextrin, 6A-deoxy-6A-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

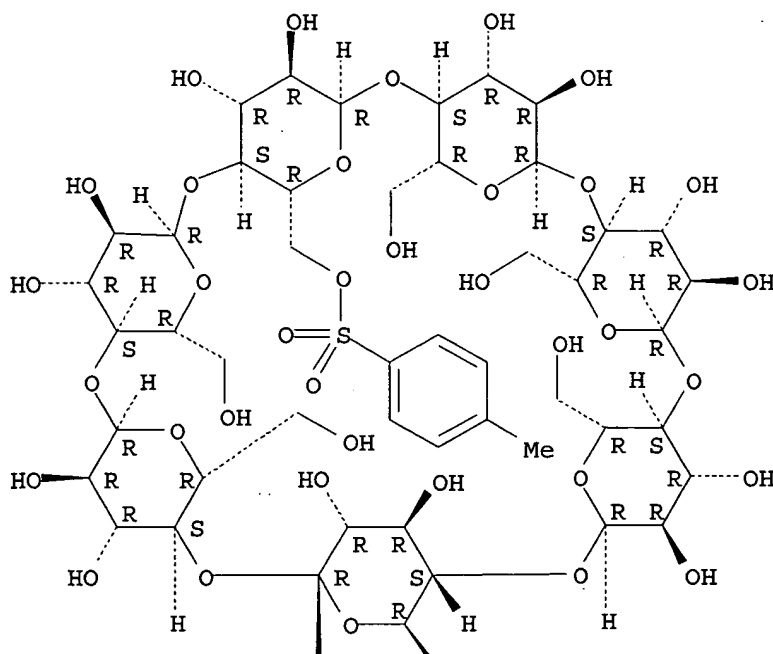


RN 67217-55-4 HCAPLUS

CN β -Cyclodextrin, 6A-(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



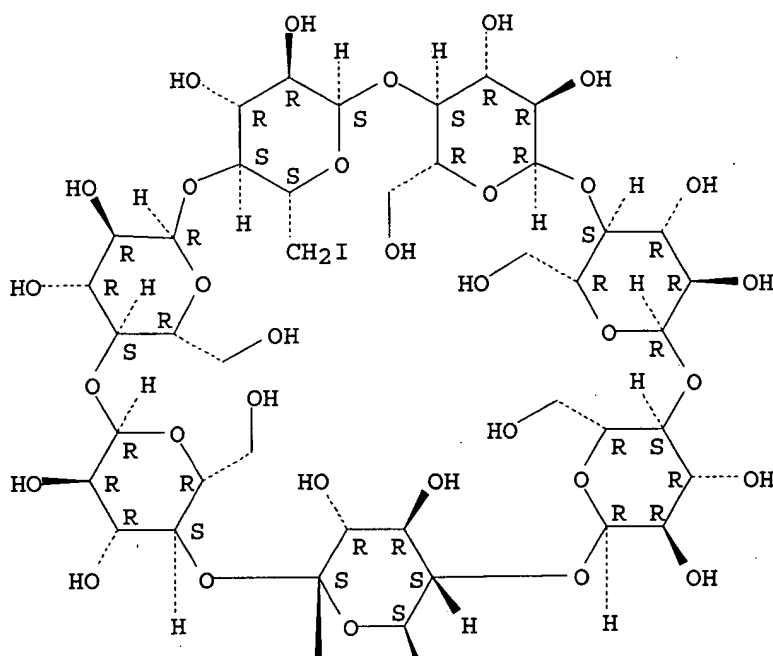
PAGE 2-A



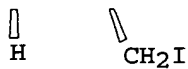
RN 76700-72-6 HCAPLUS
CN β -Cyclodextrin, 6A,6D-dideoxy-6A,6D-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



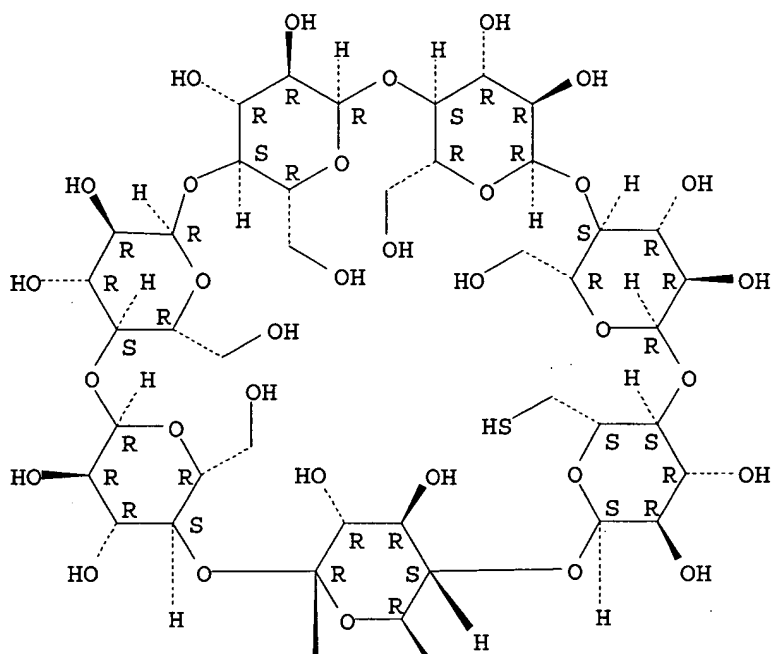
PAGE 2-A



RN 81644-55-5 HCAPLUS
CN β-Cyclodextrin, 6A-thio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



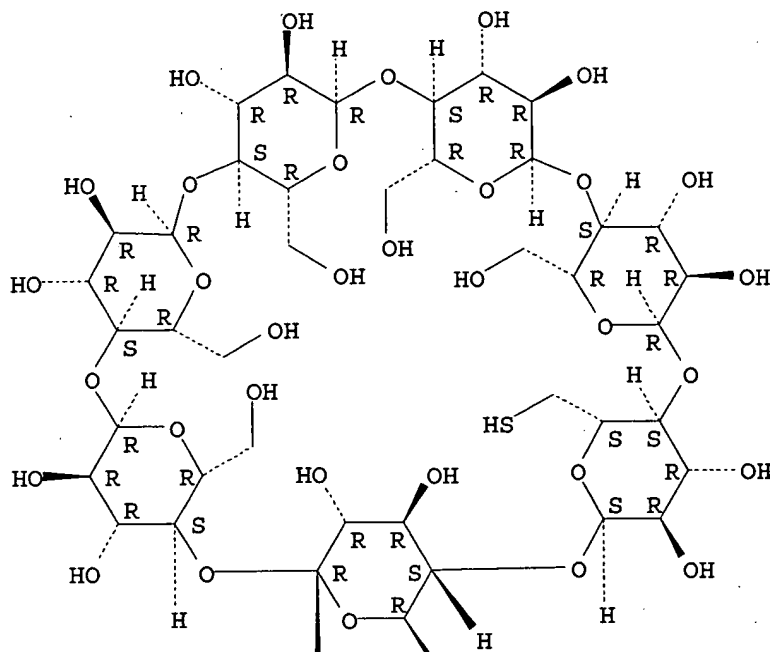
PAGE 2-A



RN 81644-55-5 HCAPLUS
CN β -Cyclodextrin, 6A-thio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

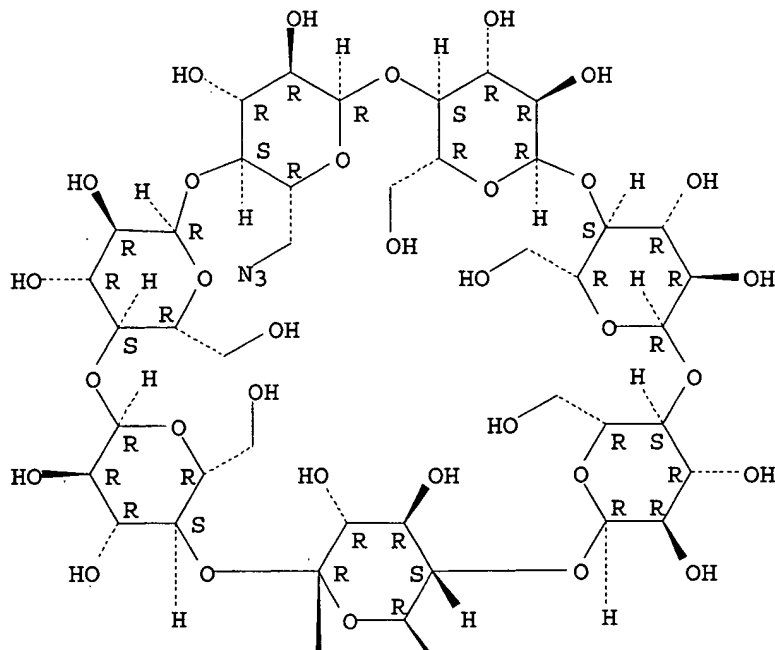


RN 98126-99-9 HCAPLUS

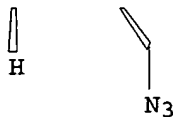
CN β -Cyclodextrin, 6A,6D-diazido-6A,6D-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



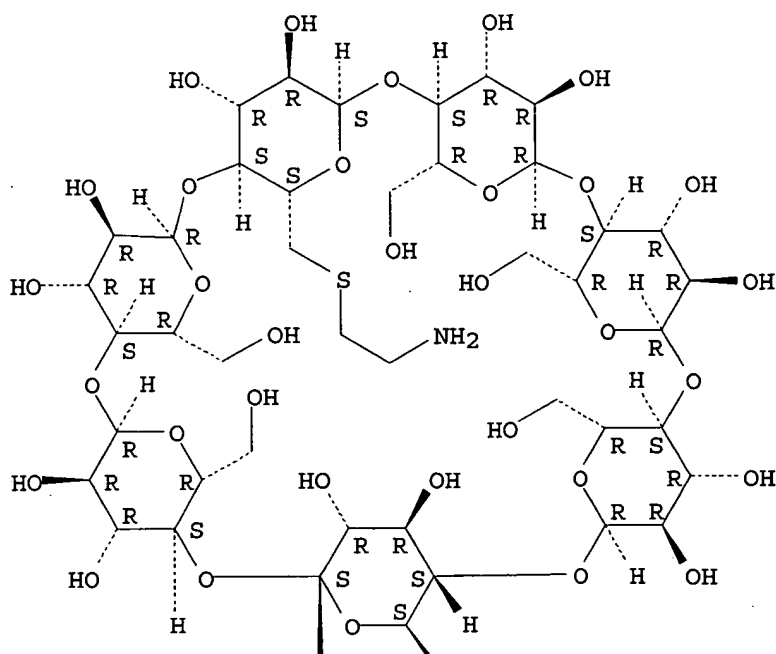
PAGE 2-A



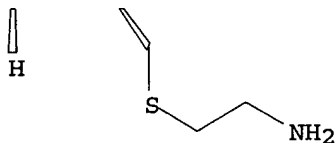
RN 101652-40-8 HCAPLUS
CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



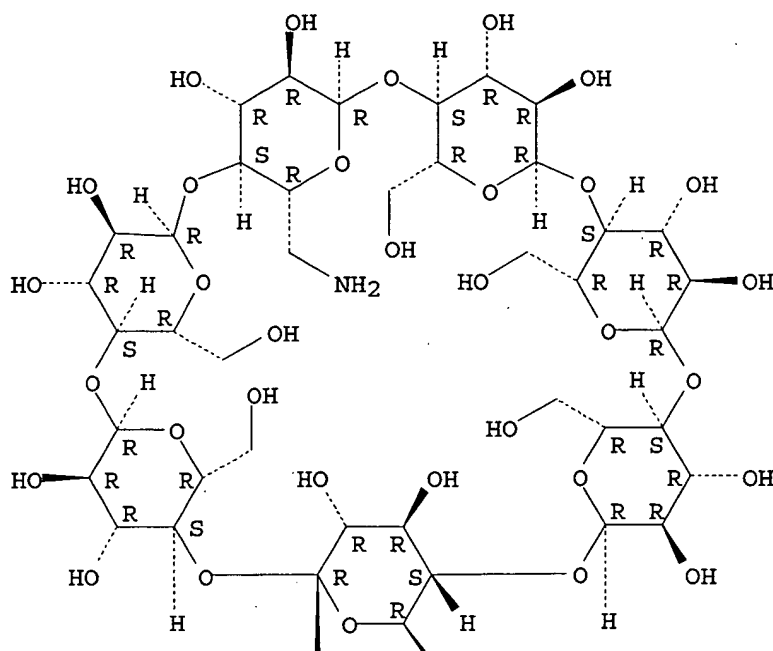
RN 254912-03-3 HCAPLUS
 CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2) (9CI)
 (CA INDEX NAME)

CM 1

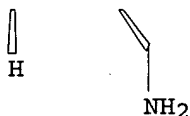
CRN 162825-08-3
 CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



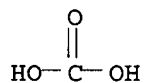
PAGE 2-A



CM 2

CRN 463-79-6

CMF C H2 O3



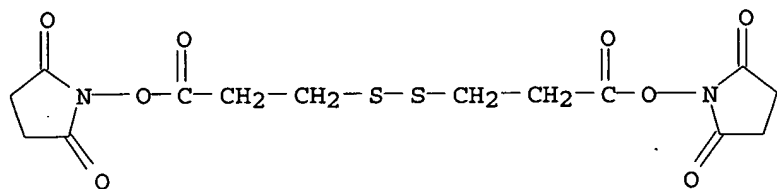
RN 254912-04-4 HCAPLUS

CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2),
polymer with 1,1'-[dithiobis[(1-oxo-3,1-propanediyl)oxy]]bis[2,5-
pyrrolidinedione] (9CI) (CA INDEX NAME)

CM 1

CRN 57757-57-0

CMF C14 H16 N2 O8 S2



CM 2

CRN 254912-03-3

CMF C42 H72 N2 O33 . 2 C H2 O3

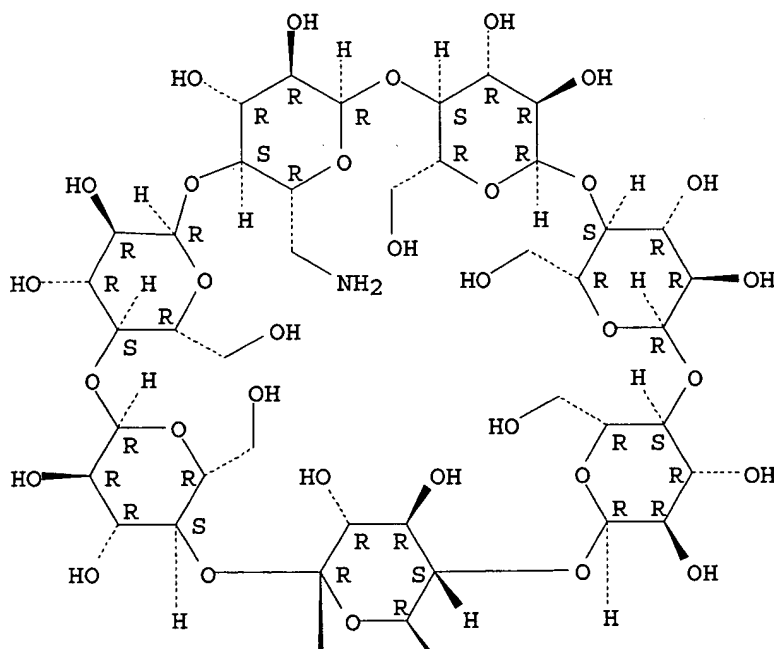
CM 3

CRN 162825-08-3

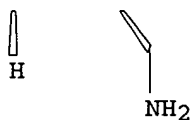
CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



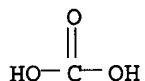
PAGE 2-A



CM 4

CRN 463-79-6

CMF C H2 O3



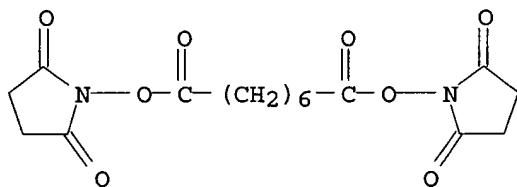
RN 254912-05-5 HCAPLUS

CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2),
polymer with 1,1'-[(1,8-dioxo-1,8-octanediyl)bis(oxy)]bis[2,5-
pyrrolidinedione] (9CI) (CA INDEX NAME)

CM 1

CRN 68528-80-3

CMF C16 H20 N2 O8



CM 2

CRN 254912-03-3

CMF C42 H72 N2 O33 . 2 C H2 O3

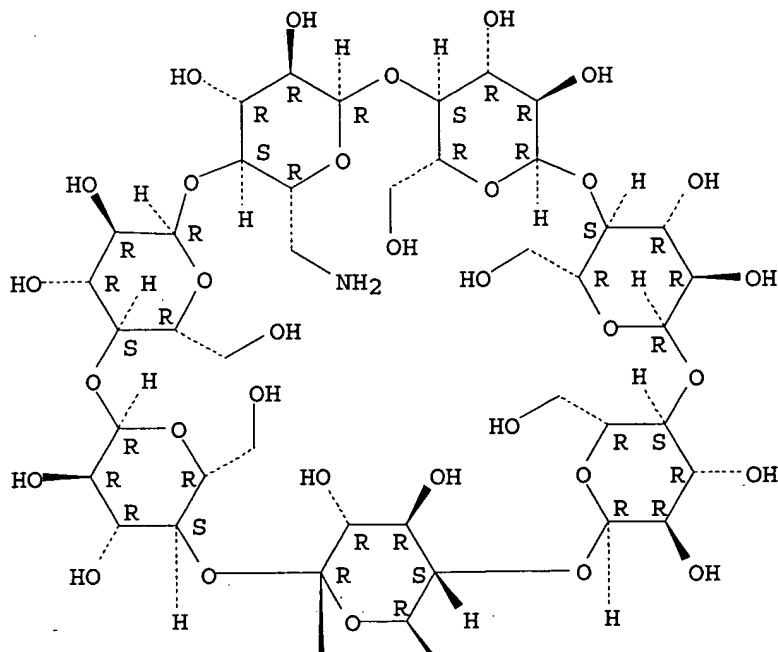
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CRN 162825-08-3

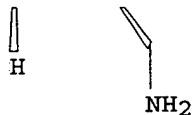
CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



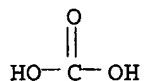
PAGE 2-A



CM 4

CRN 463-79-6

CMF C H2 O3



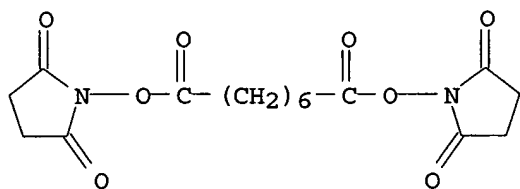
RN 254912-05-5 HCAPLUS

CN β-Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2),
polymer with 1,1'-[(1,8-dioxo-1,8-octanediyl)bis(oxy)]bis[2,5-
pyrrolidinedione] (9CI) (CA INDEX NAME)

CM 1

CRN 68528-80-3

CMF C16 H20 N2 O8



CM 2

CRN 254912-03-3

CMF C42 H72 N2 O33 . 2 C H2 O3

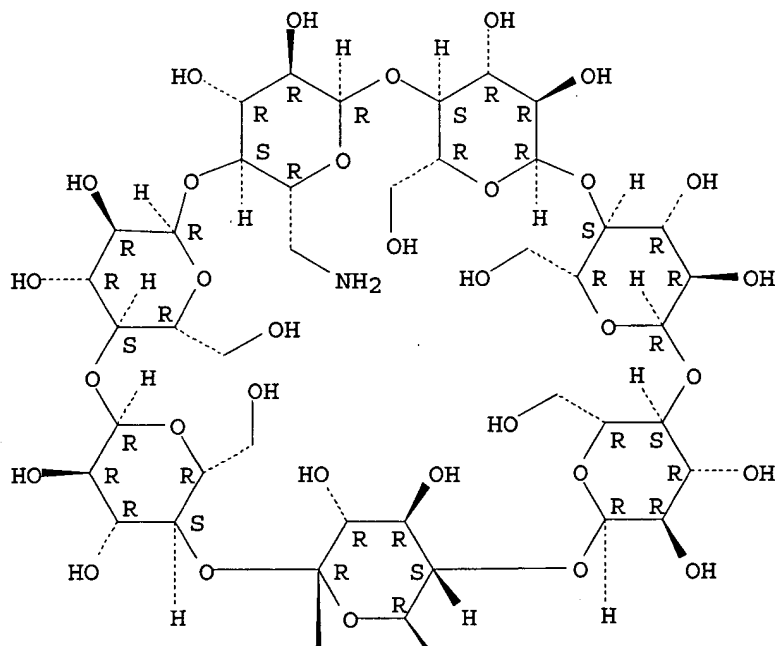
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CRN 162825-08-3

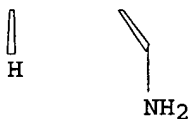
CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



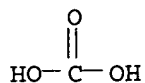
PAGE 2-A



CM 4

CRN 463-79-6

CMF C H2 O3



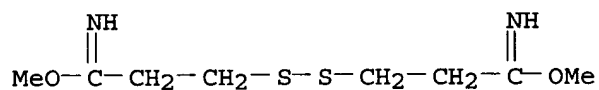
RN 254912-07-7 HCAPLUS

CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2),
polymer with dimethyl 3,3'-dithiobis[propanimidate] dihydrochloride (9CI)
(CA INDEX NAME)

CM 1

CRN 38285-78-8

CMF C8 H16 N2 O2 S2 . 2 Cl H



● 2 HCl

CM 2

CRN 254912-03-3

CMF C42 H72 N2 O33 . 2 C H2 O3

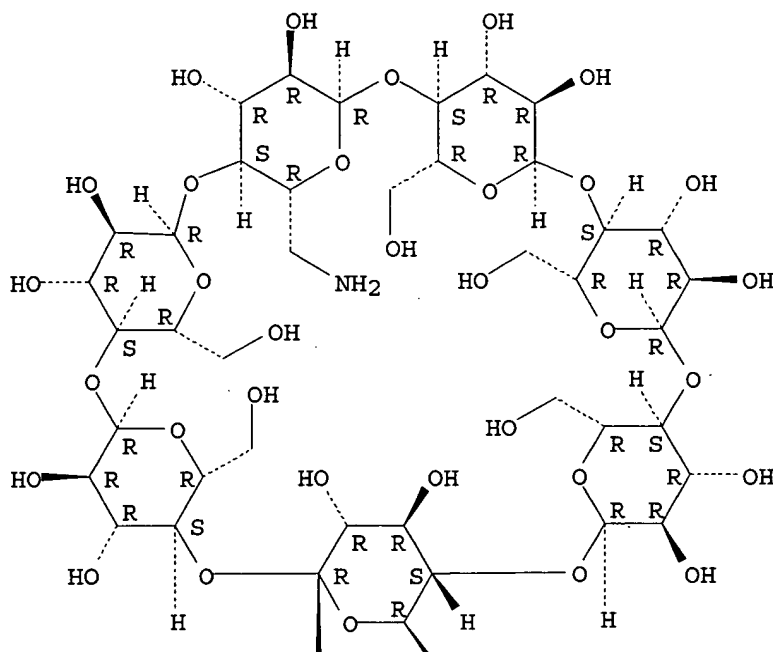
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CRN 162825-08-3

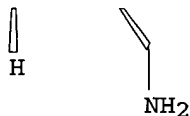
CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



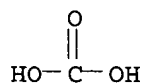
PAGE 2-A



CM 4

CRN 463-79-6

CMF C H2 O3



RN 254912-09-9 HCAPLUS

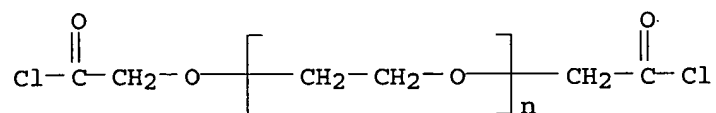
CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2),
polymer with α -(2-chloro-2-oxoethyl)- ω -(2-chloro-2-oxoethoxy)poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

CM 1

CRN 35625-91-3

CMF (C2 H4 O)_n C4 H4 Cl2 O3

CCI PMS



CM 2

CRN 254912-03-3

CMF C42 H72 N2 O33 . 2 C H2 O3

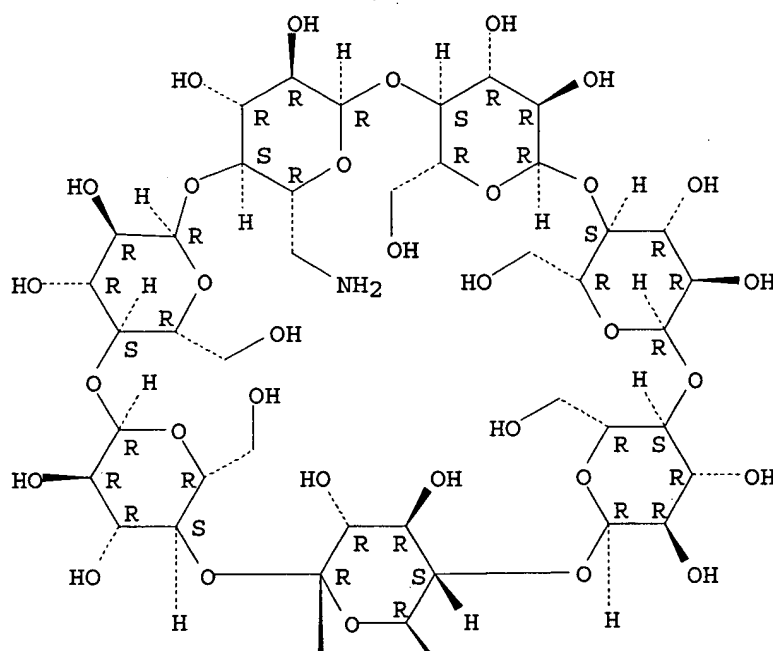
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CRN 162825-08-3

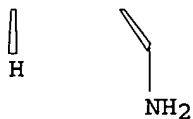
CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



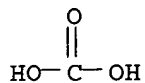
PAGE 2-A



CM 4

CRN 463-79-6

CMF C H2 O3



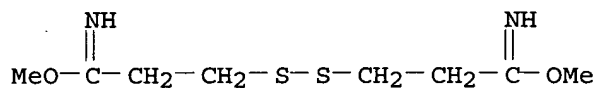
RN 275354-52-4 HCAPLUS

CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, carbonate
(1:2) (salt), polymer with dimethyl 3,3'-dithiobis[propanimidate]
dihydrochloride (9CI) (CA INDEX NAME)

CM 1

CRN 38285-78-8

CMF C8 H16 N2 O2 S2 . 2 Cl H



●2 HCl

CM 2

CRN 275354-51-3

CMF C46 H80 N2 O33 S2 . 2 C H2 O3

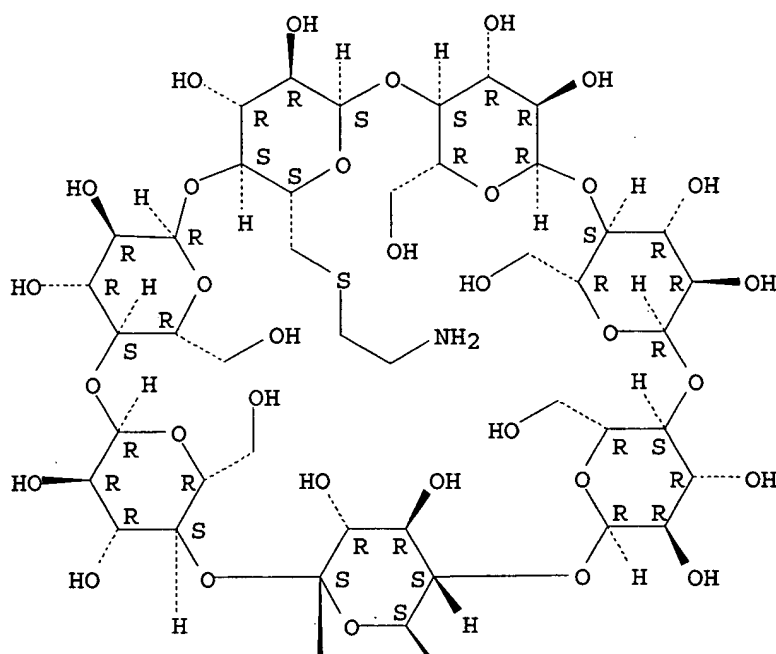
CM 3

CRN 101652-40-8

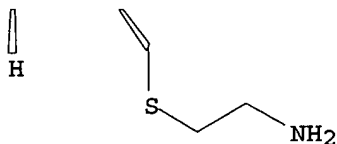
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

PAGE 1-A



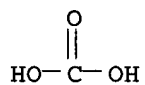
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CM 4

CRN 463-79-6

CMF C H2 O3



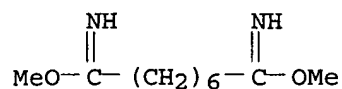
RN 275354-53-5 HCAPLUS

CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, carbonate
(1:2) (salt), polymer with dimethyl octanediimide dihydrochloride (9CI)
(CA INDEX NAME)

CM 1

CRN 34490-86-3

CMF C10 H20 N2 O2 . 2 Cl H



●2 HCl

CM 2

CRN 275354-51-3

CMF C46 H80 N2 O33 S2 . 2 C H2 O3

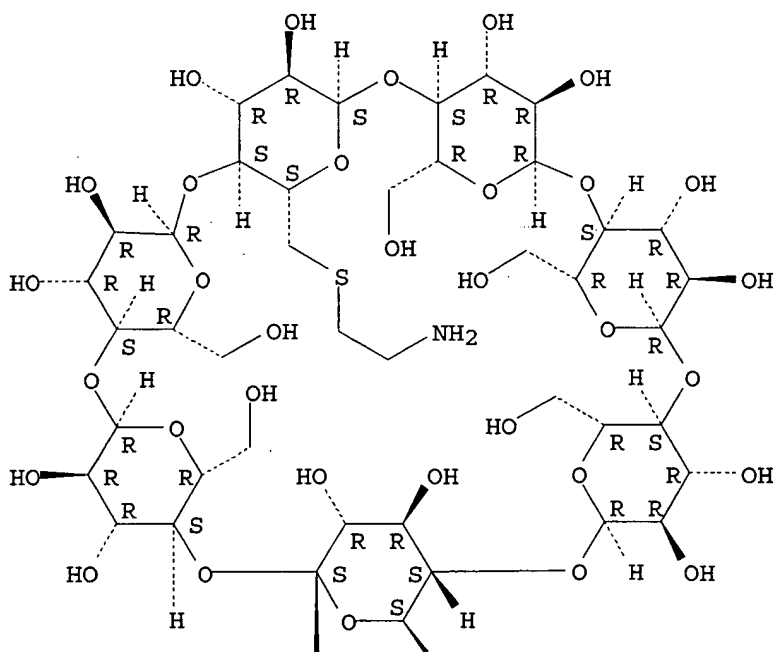
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CRN 101652-40-8

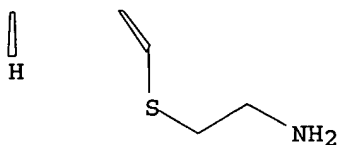
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

PAGE 1-A



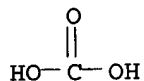
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CM 4

CRN 463-79-6

CMF C H2 O3



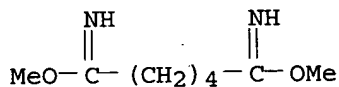
RN 275354-54-6 HCAPLUS

CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, carbonate
(1:2) (salt), polymer with dimethyl hexanediimide dihydrochloride (9CI)
(CA INDEX NAME)

CM 1

CRN 14620-72-5

CMF C8 H16 N2 O2 . 2 Cl H



● 2 HCl

CM 2

CRN 275354-51-3

CMF C46 H80 N2 O33 S2 . 2 C H2 O3

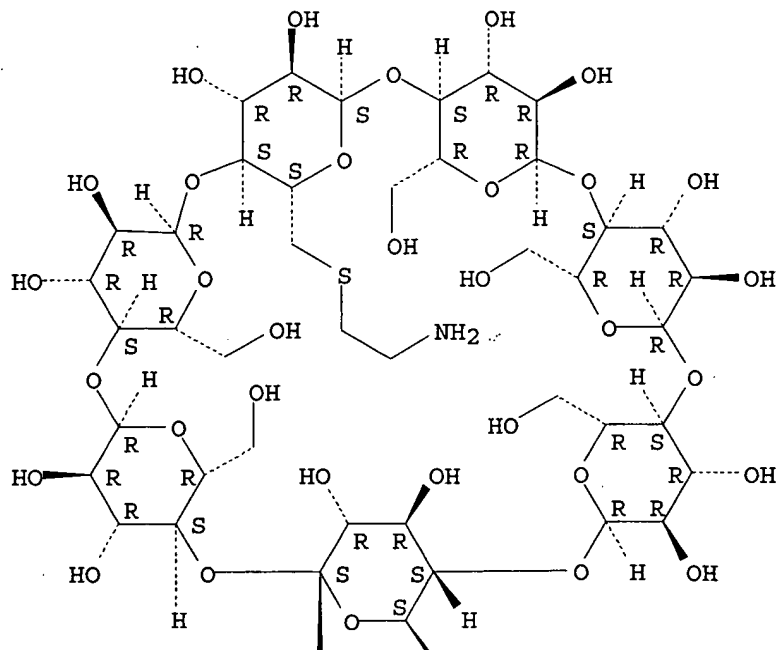
CM 3

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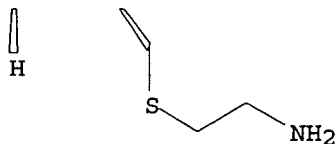
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

PAGE 1-A



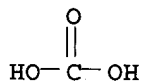
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CM 4

CRN 463-79-6

CMF C H2 O3



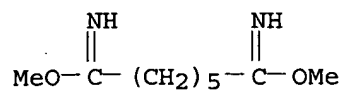
RN 275354-55-7 HCAPLUS

CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, carbonate
(1:2) (salt), polymer with dimethyl heptanediimide dihydrochloride (9CI)
(CA INDEX NAME)

CM 1

CRN 58537-94-3

CMF C9 H18 N2 O2 . 2 Cl H



●2 HCl

CM 2

CRN 275354-51-3

CMF C46 H80 N2 O33 S2 . 2 C H2 O3

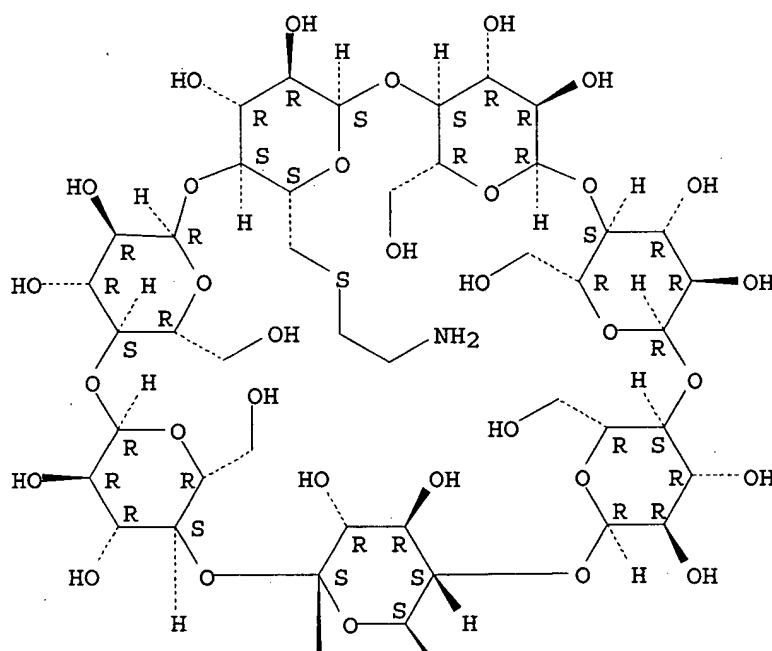
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CRN 101652-40-8

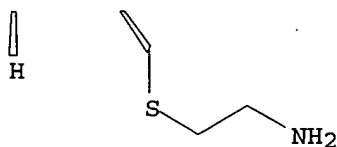
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

PAGE 1-A



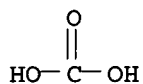
PAGE 2-A



CM 4

CRN 463-79-6

CMF C H2 O3



RN 275354-57-9 HCAPLUS

CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio-, polymer
with α -(chloroacetyl)- ω -[(chloroacetyl)oxy]poly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

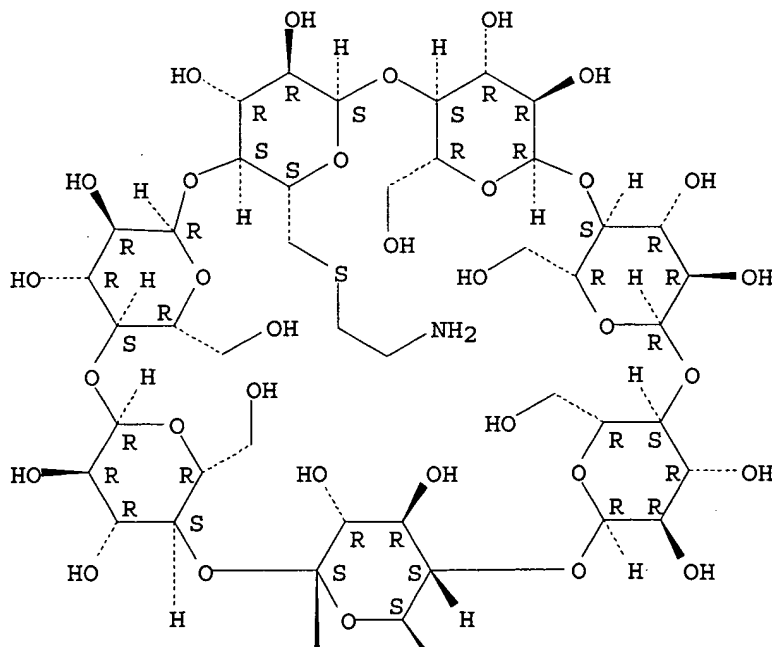
CM 1

CRN 101652-40-8

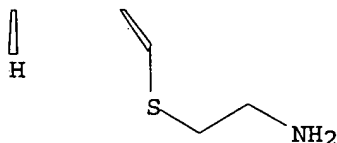
CMF C46 H80 N2 O33 S2

Absolute stereochemistry.

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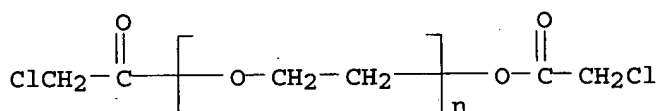


CM 2

CRN 56867-89-1

CMF (C2 H4 O)_n C4 H4 Cl2 O3

CCI PMS



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:34909 HCAPLUS

DOCUMENT NUMBER: 132:94914

TITLE: Preparation of **linear** cyclodextrin **copolymers**

INVENTOR(S): Gonzalez, Hector; Hwang, Suzie Sue Jean; Davis, Mark E.

PATENT ASSIGNEE(S): California Institute of Technology, USA

SOURCE: PCT Int. Appl., 84 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000001734	A1	20000113	WO 1999-US14298	19990625
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6509323	B1	20030121	US 1998-203556	19981202
CA 2336390	AA	20000113	CA 1999-2336390	19990625
AU 9948305	A1	20000124	AU 1999-48305	19990625
AU 763114	B2	20030710		

Appel's own work

EP 1093469 A1 20010425 EP 1999-931889 19990625
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI

BR 9911754 A 20011106 BR 1999-11754 19990625
 JP 2002519482 T2 20020702 JP 2000-558134 19990625
 US 2002151523 A1 20021017 US 2002-97326 20020315

PRIORITY APPLN. INFO.:

US 1998-91550P P 19980701
 US 1998-203556 A 19981202
 US 1999-339818 A3 19990625
 WO 1999-US14298 W 19990625

AB **Linear cyclodextrin copolymers** containing an unoxidized and/or an oxidized cyclodextrin moiety integrated into the polymer backbone, useful as drug delivery vehicles, were prepared. For example, substitution reaction of 6A,6D-diiodo-6A,6D-deoxy- β -cyclodextrin (2-step preparation by a known procedure given) with NaSCH₂CH₂NH₂ gave 79% 6A,6D-bis(2-aminoethylthio)-6A6D-deoxy- β -cyclodextrin. This was stirred for 18 h at 80° in DMF under N with an equiv of MeOC(:NH)(CH₂)₆C(:NH)OMe-2HCl in the presence of Et₃N to give 18% of a title copolymer (CD copolymer). Media containing doxorubicin and CD copolymer-doxorubicin complex (general complexation procedure given) were applied to cultured cell lines to show no toxicity to KB or KB-VI cell lines in the absence of doxorubicin.

IC ICM C08B037-16

ICS C08G081-00; C08G069-00; C08G069-40; C08G073-02; C08G073-06;
 C08G075-00; A61K047-40

CC 44-6 (Industrial Carbohydrates)

Section cross-reference(s): 63

ST cyclodextrin **linear copolymer** prepn drug delivery;
 iododeoxycyclodextrin prepn substitution aminoethylthiocyclodextrin;
 aminoethylthiocyclodextrin prepn polymn dimethylsuberimide; doxorubicin
 complex aminoethylthiocyclodextrin dimethylsuberimide copolymer cell
 toxicity

IT Drug delivery systems

(preparation of **linear cyclodextrin copolymers** as)

IT 51178-68-8

RL: RCT (Reactant); RACT (Reactant or reagent)
 (acid chlorination; preparation of **linear cyclodextrin
 copolymers** as drug delivery agents)

IT 91190-86-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and conversion to diiodo derivative; preparation of **linear
 cyclodextrin copolymers** as drug delivery agents)

IT 35625-91-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and copolymn. with diaminocyclodextrin; preparation of
linear cyclodextrin copolymers as drug delivery
 agents)

IT 101652-40-8P 254912-03-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation and copolymn.; preparation of **linear
 cyclodextrin copolymers** as drug delivery agents)

IT 98126-99-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation and redn to diamine; preparation of **linear cyclodextrin
 copolymers** as drug delivery agents)

IT 76700-72-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and substitution with sodium azide; preparation of linear cyclodextrin copolymers as drug delivery agents)

IT 23214-92-8DP, Doxorubicin, complexes with cyclodextrin copolymers
RL: BSU (Biological study, unclassified); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
(preparation of linear cyclodextrin copolymers as drug delivery agents)

IT 254912-04-4P 254912-05-5DP, oxidized 254912-05-5P 254912-07-7P
254912-08-8P 254912-09-9P 254912-10-2P 254912-11-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of linear cyclodextrin copolymers as drug delivery agents)

IT 7585-39-9, β -Cyclodextrin
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with biphenyldisulfonyl dichloride; preparation of linear cyclodextrin copolymers as drug delivery agents)

IT 3406-84-6, Biphenyl-4,4'-disulfonyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with β -cyclodextrin; preparation of linear cyclodextrin copolymers as drug delivery agents)

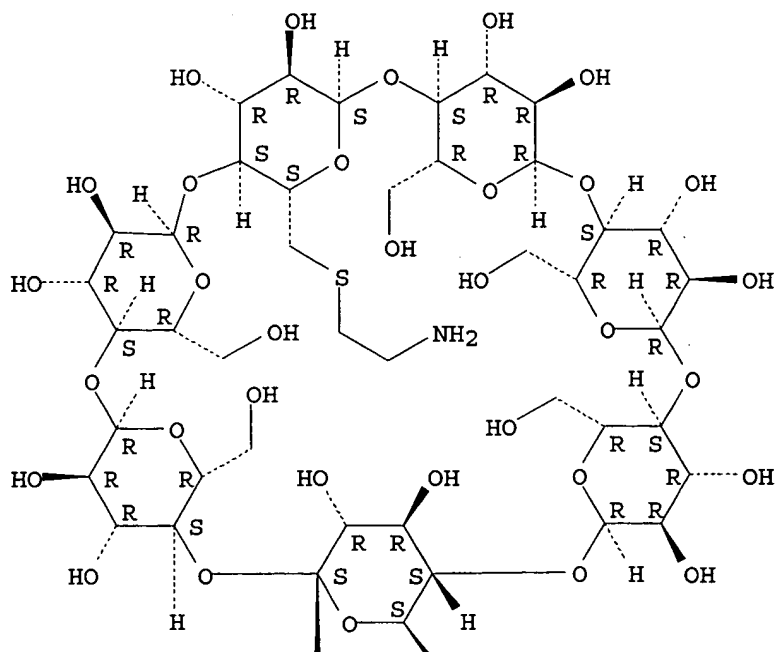
IT 51974-68-6, Sodium 2-aminoethylthiolate
RL: RCT (Reactant); RACT (Reactant or reagent)
(thioetherification of diiodocyclodextrin; preparation of linear cyclodextrin copolymers as drug delivery agents)

IT 101652-40-8P 254912-03-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and copolymn.; preparation of linear cyclodextrin copolymers as drug delivery agents)

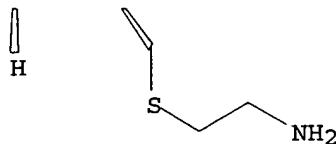
RN 101652-40-8 HCAPLUS
CN β -Cyclodextrin, 6A,6D-bis-S-(2-aminoethyl)-6A,6D-dithio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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RN 254912-03-3 HCAPLUS

CN β -Cyclodextrin, 6A,6D-diamino-6A,6D-dideoxy-, carbonate (1:2) (9CI)
(CA INDEX NAME)

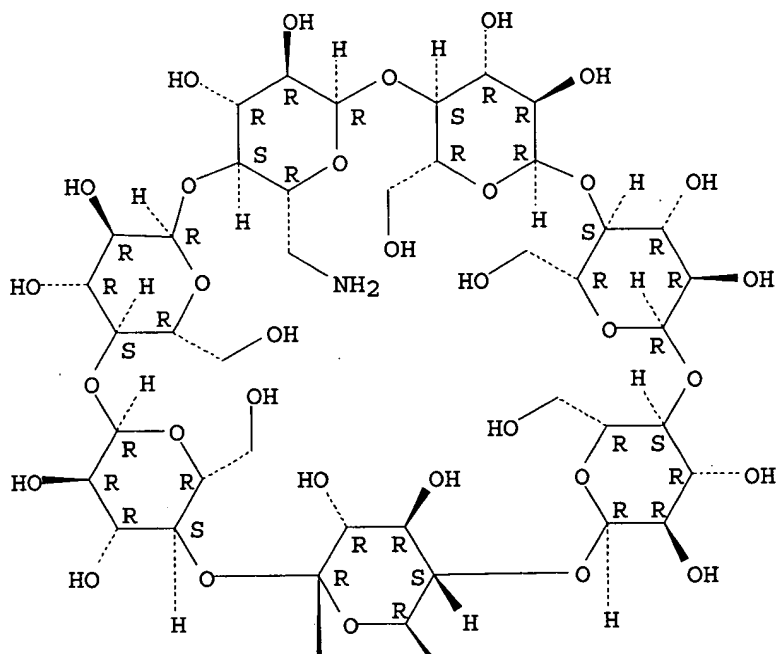
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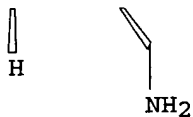
CMF C42 H72 N2 O33

Absolute stereochemistry.

PAGE 1-A



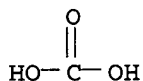
PAGE 2-A



CM 2

CRN 463-79-6

CMF C H2 O3



IT 98126-99-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

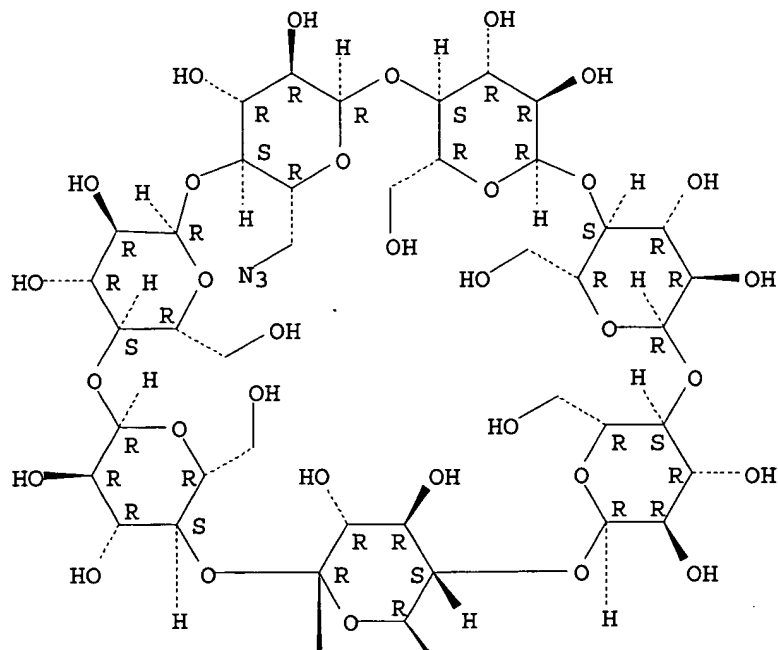
(preparation and redn to diamine; preparation of linear cyclodextrin
copolymers as drug delivery agents)

RN 98126-99-9 HCAPLUS

CN β -Cyclodextrin, 6A,6D-diazo-6A,6D-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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IT 76700-72-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

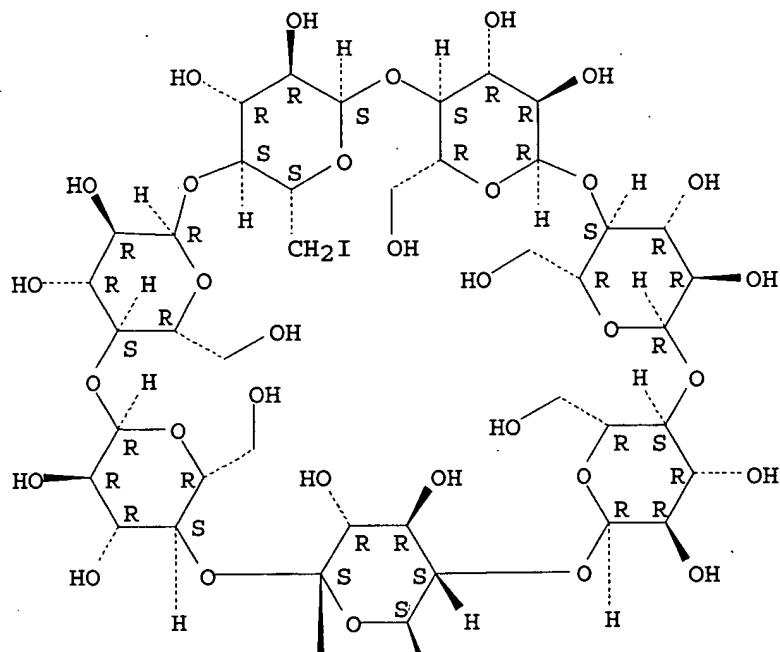
(preparation and substitution with sodium azide; preparation of linear cyclodextrin copolymers as drug delivery agents)

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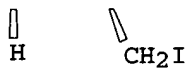
CN β -Cyclodextrin, 6A,6D-dideoxy-6A,6D-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT